```
=> d his

     (FILE 'REGISTRY' ENTERED AT 09:14:25 ON 09 JAN 2003)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 09:16:29 ON 09 JAN 2003
               ACT GUO/A
               ---------
L1              STR
L2              SCR 1992 OR 1839 OR 2021 OR 2026
L3          726 SEA FILE=REGISTRY SSS FUL L1 NOT L2
               ---------
               ACT GUOENZYME/A
               ---------
L4   (        1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 2.7.1.137"/CN
L5   (        2)SEA FILE=REGISTRY ABB=ON  PLU=ON  ("E.C. 2.7.1.67"/CN OR "E.C.
L6   (        3)SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5
L7   (        1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 3.1.3.36"/CN
L8   (        1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 3.1.3.64"/CN
L9   (        2)SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 OR L8
L10  (        2)SEA FILE=REGISTRY ABB=ON  PLU=ON  ("E.C. 3.1.4.10"/CN OR "E.C.
L11           7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 OR L9 OR L6
               ---------


     FILE 'HCAPLUS' ENTERED AT 09:29:23 ON 09 JAN 2003
L12         529 S L3
L13       10081 S L11
L14          42 S L12 AND L13
L15      192697 S ASSAY? OR IMMUNOASSAY? OR IMMUNOCHEMICAL? OR IMMOBILI?
L16           2 S L14 AND L15
L17       25885 S S ALDEHYDE? OR LABEL? (L) PHOSPH? OR SCINTILLA? OR PHOSPHOIMA
L18       12858 S AVIDIN# OR BIOTIN# OR STERPAVIDIN?
L19           1 S L14 AND (L17 OR L18)
L20           2 S L19 OR L16

     FILE 'REGISTRY' ENTERED AT 09:31:58 ON 09 JAN 2003
               E PHOSPHORUS/CN
L21           2 S PHOSPHORUS AND ISOTOPE AND 32

     FILE 'HCAPLUS' ENTERED AT 09:34:39 ON 09 JAN 2003
L22           4 S L21 AND L13
L23          60 S L13 (L) L15
L24           2 S L23 AND L17
L25           2 S L23 AND L18
L26           6 S L22 OR L24 OR L25
L27           7 S L20 OR L26
L28           1 S L23 AND KIT#
L29         136 S L13 AND L15
L30          19 S L29 AND (L17 OR L18 OR KIT#)
L31          16 S L30 NOT (L27 OR L28)
L32        2462 S 32P OR P 32
L33           8 S L32 AND L13
L34           6 S L33 AND (L15 OR L17 OR L18 OR KIT#)
L35           3 S L34 NOT (L31 OR L27 OR L28)
L36         410 S (EC OR E C ) (W) (3 1 3 OR 3 1 4 OR 2 7 1)
L37           1 S L36 AND L12
```

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=> fil reg
FILE 'REGISTRY' ENTERED AT 09:39:36 ON 09 JAN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     7 JAN 2003  HIGHEST RN 478336-86-6
DICTIONARY FILE UPDATES:    7 JAN 2003  HIGHEST RN 478336-86-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d que stat l3
L1              STR
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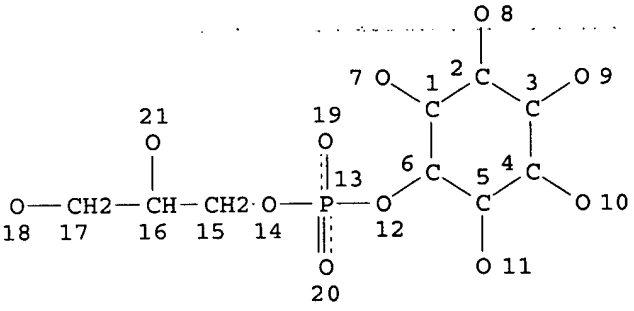

Structure cl. 7

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L2              SCR 1992 OR 1839 OR 2021 OR 2026
L3          726 SEA FILE=REGISTRY SSS FUL L1 NOT L2

100.0% PROCESSED    905 ITERATIONS                      726 ANSWERS
SEARCH TIME: 00.00.26


=> d que l11
L4   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 2.7.1.137"/CN
L5   (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  ("E.C. 2.7.1.67"/CN OR "E.C.
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                2.7.1.68"/CN)
L6   (          3) SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5
L7   (          1) SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 3.1.3.36"/CN
L8   (          1) SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 3.1.3.64"/CN
L9   (          2) SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 OR L8
L10  (          2) SEA FILE=REGISTRY ABB=ON  PLU=ON  ("E.C. 3.1.4.10"/CN OR "E.C.
                3.1.4.11"/CN)
L11             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 OR L9 OR L6
```

=> d l11 ide can 1-7 enzymes claimed in application

L11 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2003 ACS unable to find e.c. 3.13.67
RN 124248-47-1 REGISTRY
CN Phosphatase, phosphatidylinositol 3- (9CI) (CA INDEX NAME) or e.c. 3.13.27
OTHER NAMES:
CN **E.C. 3.1.3.64**
CN Phosphatidylinositol 3-phosphatase
CN Phosphatidylinositol 3-phosphate 3-phosphatase
CN Phosphoinositide 3-phosphatase
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
16 REFERENCES IN FILE CA (1962 TO DATE)
16 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:182120

REFERENCE 2: 137:182119

REFERENCE 3: 137:107512

REFERENCE 4: 136:335785

REFERENCE 5: 136:307832

REFERENCE 6: 136:228713

REFERENCE 7: 136:66032

REFERENCE 8: 136:17258

REFERENCE 9: 132:277900

REFERENCE 10: 132:106220

L11 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2003 ACS
RN 115926-52-8 REGISTRY
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **E.C. 2.7.1.137**
CN Phosphatidylinositol 3'-kinase
CN Phosphatidylinositol 3-hydroxyl kinase
CN Phosphatidylinositol 3-kinase
CN Phosphoinositide 3'-hydroxykinase
CN Phosphoinositide 3'-kinase
CN Phosphoinositide 3-kinase

CN PI3 kinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
6348 REFERENCES IN FILE CA (1962 TO DATE)
37 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6406 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:13350

REFERENCE 2: 138:13345

REFERENCE 3: 138:12924

REFERENCE 4: 138:12900

REFERENCE 5: 138:12890

REFERENCE 6: 138:12884

REFERENCE 7: 138:11823

REFERENCE 8: 138:11800

REFERENCE 9: 138:11783

REFERENCE 10: 138:11756

L11 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2003 ACS
RN 104645-76-3 REGISTRY
CN Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Diphosphodiglyceride inositol kinase
CN Diphosphoinositide kinase
CN **E.C. 2.7.1.68**
CN Gene MSS4 kinases
CN Kinase, gene MSS4
CN MSS4
CN Phosphatidylinositol 4-monophosphate 5-kinase
CN Phosphatidylinositol 4-monophosphate kinase
CN Phosphatidylinositol 4-phosphate 5-kinase
CN Phosphatidylinositol 4-phosphate 5-kinase C
CN Phosphatidylinositol 4-phosphate kinase
DR 9032-61-5
MF Unspecified
CI MAN
SR CA
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
162 REFERENCES IN FILE CA (1962 TO DATE)
164 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:380648

REFERENCE 2: 137:308236

REFERENCE 3: 137:307382

REFERENCE 4: 137:273158

REFERENCE 5: 137:214041

REFERENCE 6: 137:199385

REFERENCE 7: 137:198067

REFERENCE 8: 137:197086

REFERENCE 9: 137:166622

REFERENCE 10: 137:90191

L11 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2003 ACS
RN 63551-76-8 REGISTRY
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Phosphatidylinositol-4,5-bisphosphate phosphodiesterase
CN **E.C. 3.1.4.11**
CN Glycoprotein VSG lipase
CN Inositol phospholipid-specific phospholipase C
CN Inositol-specific phospholipase C
CN Phosphatidyl inositol-4,5-bisphosphate phospholipase C
CN Phosphatidylinositide-phospholipase C
CN Phosphatidylinositide-specific phospholipase C
CN Phosphatidylinositol 4-monophosphate-phospholipase C
CN Phosphatidylinositol bisphosphate phospholipase C
CN Phosphatidylinositol phospholipase C
CN Phosphatidylinositol-4,5-bisphosphate-specific phospholipase C
CN Phosphatidylinositol-dependent phospholipase C
CN Phosphatidylinositol-sensitive phospholipase C
CN Phosphatidylinositol-specific phospholipase C
CN Phosphoinositidase
CN Phosphoinositidase C
CN Phosphoinositide phospholipase C
CN Phosphoinositide-dependent phospholipase C
CN Phosphoinositide-specific phospholipase C
CN Phosphoinositol-specific phospholipase C
CN Phospholipase C
CN Phospholipase C, glycoprotein VSG
CN Phospholipase C-.beta.4c
CN Phospholipase C.alpha.
CN Polyphosphoinositide-phospholipase C
CN Polyphosphoinositide-specific phospholipase C
CN Polyphosphoinositol-specific phospholipase C
CN Triphosphoinositide phosphodiesterase
DR 105503-68-2, 37213-51-7
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2940 REFERENCES IN FILE CA (1962 TO DATE)

12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2956 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:13350

REFERENCE 2: 138:12416

REFERENCE 3: 138:11769

REFERENCE 4: 138:11705

REFERENCE 5: 138:3063

REFERENCE 6: 138:2674

REFERENCE 7: 138:2210

REFERENCE 8: 138:981

REFERENCE 9: 138:211

REFERENCE 10: 137:383009

L11 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2003 ACS
RN 37288-19-0 REGISTRY
CN Phosphodiesterase, monophosphatidylinositol (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **E.C. 3.1.4.10**
CN Monophosphatidylinositol phosphodiesterase
CN Phosphatidylinositol phosphodiesterase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
53 REFERENCES IN FILE CA (1962 TO DATE)
53 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:380851

REFERENCE 2: 136:17258

REFERENCE 3: 131:240068

REFERENCE 4: 125:321256

REFERENCE 5: 122:76137

REFERENCE 6: 116:210062

REFERENCE 7: 111:111105

REFERENCE 8: 108:183200

REFERENCE 9: 107:110772

REFERENCE 10: 107:35461

L11 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 37205-54-2 REGISTRY
CN Kinase (phosphorylating), phosphatidylinositol 4- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Phosphatidylinositol 4-kinase
CN **E.C. 2.7.1.67**
CN Phosphatidylinositol 4-kinase
CN Polyphosphoinositide 4-kinase
DR 115603-35-5
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
579 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
581 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:884

REFERENCE 2: 137:382634

REFERENCE 3: 137:382625

REFERENCE 4: 137:366873

REFERENCE 5: 137:348008

REFERENCE 6: 137:321245

REFERENCE 7: 137:320531

REFERENCE 8: 137:273469

REFERENCE 9: 137:273411

REFERENCE 10: 137:229829

L11 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2003 ACS
RN 9036-01-5 REGISTRY
CN Phosphatase, triphosphoinositide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Diphosphoinositide phosphatase
CN **E.C. 3.1.3.36**
CN Phosphatidylinositol 4,5-bisphosphate 5-phosphatase
CN Phosphatidylinositol bisphosphatase
CN Triphosphoinositide phosphatase
CN Triphosphoinositide phosphomonoesterase
DR 54596-22-4
MF Unspecified
CI MAN
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
68 REFERENCES IN FILE CA (1962 TO DATE)
70 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:884

REFERENCE 2: 136:81813

REFERENCE 3: 136:17258

REFERENCE 4: 135:329830

REFERENCE 5: 135:41513

REFERENCE 6: 133:57121

REFERENCE 7: 132:277413

REFERENCE 8: 132:90950

REFERENCE 9: 130:122592

REFERENCE 10: 129:201654

=>

=> d que l21
L21 2 SEA FILE=REGISTRY ABB=ON PLU=ON PHOSPHORUS AND ISOTOPE AND
32

=> d l21 ide can 1-2

L21 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 20193-14-0 REGISTRY
CN **Phosphorus, isotope of mass 32 (32P1-) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Phosphorus, isotope of mass 32, ion (P1-) (8CI)**
OTHER NAMES:
CN 32P1-
CN **Phosphorus-32(1+)**
MF P
LC STN Files: AGRICOLA, CA, CAPLUS

32p+

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 91:46102

REFERENCE 2: 90:196426

REFERENCE 3: 76:6783

L21 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 14596-37-3 REGISTRY
CN **Phosphorus, isotope of mass 32 (8CI, 9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 32P
CN **P 32**
CN **Phosphorus-32**
DR 24267-55-8

MF P
CI COM
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSNB, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, NIOSHTIC, PROMT, TOXCENTER, USPAT2, USPATFULL

32p

2922 REFERENCES IN FILE CA (1962 TO DATE)
87 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2923 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:16685

REFERENCE 2: 138:16683

REFERENCE 3: 138:12389

REFERENCE 4: 138:11413

REFERENCE 5: 138:8325

REFERENCE 6: 138:1157

REFERENCE 7: 138:344

REFERENCE 8: 137:388726

REFERENCE 9: 137:384244

REFERENCE 10: 137:383800

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:40:26 ON 09 JAN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 9 Jan 2003 VOL 138 ISS 2
FILE LAST UPDATED: 8 Jan 2003 (20030108/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For

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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his l8-l20;d que l22-

     (FILE 'REGISTRY' ENTERED AT 09:16:29 ON 09 JAN 2003)
L8   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "E.C. 3.1.3.64"/CN
L9   (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 OR L8
L10  (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  ("E.C. 3.1.4.10"/CN OR "E.C.
L11            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 OR L9 OR L6

L12          529 S L3
L13        10081 S L11
L14           42 S L12 AND L13
L15       192697 S ASSAY? OR IMMUNOASSAY? OR IMMUNOCHEMICAL? OR IMMOBILI?
L16            2 S L14 AND L15
L17        25885 S S ALDEHYDE? OR LABEL? (L) PHOSPH? OR SCINTILLA? OR PHOSPHOIMA
L18        12858 S AVIDIN# OR BIOTIN# OR STERPAVIDIN?
L19            1 S L14 AND (L17 OR L18)
L20            2 S L19 OR L16

L22            4 S L21 AND L13
L23           60 S L13 (L) L15
L24            2 S L23 AND L17
L25            2 S L23 AND L18
L26            6 S L22 OR L24 OR L25
L27            7 S L20 OR L26
L28            1 S L23 AND KIT#
L29          136 S L13 AND L15
L30           19 S L29 AND (L17 OR L18 OR KIT#)
L31           16 S L30 NOT (L27 OR L28)
L32         2462 S 32P OR P 32
L33            8 S L32 AND L13
L34            6 S L33 AND (L15 OR L17 OR L18 OR KIT#)
L35            3 S L34 NOT (L31 OR L27 OR L28)
L36          410 S (EC OR E C ) (W) (3 1 3 OR 3 1 4 OR 2 7 1)
L37            1 S L36 AND L12
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=> d .ca hitstr l27;d .ca hitstr l28;d .ca hitstr l31 1-16;d .ca hitstr l35 1-3; d .ca hitstr l37 1

L27 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:654954 HCAPLUS
DOCUMENT NUMBER: 137:190699
TITLE: Stabilized radiophosphate-labeled proteins
INVENTOR(S): Leung, Shui-on
PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6440386	B1	20020827	US 1999-347926	19990706
PRIORITY APPLN. INFO.:			US 1998-91736P P	19980706

AB The present invention relates to 32P- and 33P-labeled proteins useful for radiotherapy of human diseases. The proteins contain peptide sequences that are substrates for protein kinase enzymes and that can be radiolabeled with a protein kinase and a 32P- or 33P-labeled phosphate donor and contain an SH2 domain which serves to protect the phosphorylated protein from in vivo dephosphorylation.
IC ICM A61K051-00
ICS A61M036-14; C07K016-00; C12P021-08
NCL 424001530
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8
IT **14596-37-3D**, Phosphorus 32, proteins labeled with, biological studies 15749-66-3D, Phosphorus 33, proteins labeled with, biological studies 152478-56-3, Jak1 kinase 152478-57-4, Jak2 kinase 152646-20-3 153190-61-5, Tyk2 kinase 285561-26-4 289884-40-8 325791-48-8 325791-51-3 325791-77-3 449180-55-6 449180-56-7 449180-57-8 449180-58-9 449180-59-0 449180-60-3 449180-61-4 449180-62-5 449180-63-6 449180-64-7 449180-65-8 449180-66-9 449180-67-0 449180-68-1 449180-69-2 449180-70-5 449180-71-6 449180-72-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiophosphate-labeled proteins contg. SH2 domain useful for radiotherapy of human diseases)
IT **63551-76-8**, Phospholipase C
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma., SH2 domain; radiophosphate-labeled proteins contg. SH2 domain useful for radiotherapy of human diseases)
IT **14596-37-3D**, Phosphorus 32, proteins labeled with, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiophosphate-labeled proteins contg. SH2 domain useful for radiotherapy of human diseases)
RN 14596-37-3 HCAPLUS
CN Phosphorus, isotope of mass 32 (8CI, 9CI) (CA INDEX NAME)

32p

IT **63551-76-8**, Phospholipase C

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma., SH2 domain; radiophosphate-labeled proteins contg. SH2 domain useful for radiotherapy of human diseases)
RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:886545 HCAPLUS
DOCUMENT NUMBER: 136:17258
TITLE: Assay for kinases and phosphatases using a product immobilization
INVENTOR(S): Goueli, Said; Vidugiriene, Jolanta; Karassina, Natasha
PATENT ASSIGNEE(S): Promega Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

same family

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092560	A2	20011206	WO 2001-US17554	20010531
WO 2001092560	A3	20020801		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002028477	A1	20020307	US 2001-871424 20010531

PRIORITY APPLN. INFO.: US 2000-208405P P 20000531
OTHER SOURCE(S): MARPAT 136:17258

AB Disclosed is a method and corresponding kit for assaying the presence, activity, or both, of an enzyme classified within an enzyme classification selected from the group consisting of EC 2.7.1, EC 3.1.3, and EC 3.1.4. The method generally includes the steps of reacting an enzyme with a substrate for a time sufficient to yield phosphorylated or dephosphorylated product; contacting the product with a binding matrix, whereby product is adhered to the matrix; and then analyzing the matrix for presence of, amt. of, or both the presence and the amt. of the product fixed to the matrix, whereby the presence, the activity, or both the presence and activity of the enzyme can be detd.

IC ICM C12Q001-00
CC 7-1 (Enzymes)
IT Immobilization, molecular
Scintillation detectors
Test kits
(assay for kinases and phosphatases using product immobilization)
IT 9013-05-2, Phosphatase 9031-44-1, Kinase (phosphorylating) 9033-46-9

9036-01-5 37205-54-2 37288-19-0
63551-76-8 72060-45-8, Lipid kinase **104645-76-3**,
Phosphatidylinositol-4-phosphate 5-kinase **104645-76-3**
115926-52-8, Phosphatidylinositol 3-kinase **124248-47-1**
210488-47-4, Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase
RL: ANT (Analyte); ANST (Analytical study)
(**assay** for kinases and phosphatases using product **immobilization**)

IT **9036-01-5 37205-54-2 37288-19-0**
63551-76-8 104645-76-3, Phosphatidylinositol-4-phosphate
5-kinase **115926-52-8**, Phosphatidylinositol 3-kinase
124248-47-1
RL: ANT (Analyte); ANST (Analytical study)
(**assay** for kinases and phosphatases using product **immobilization**)

RN 9036-01-5 HCAPLUS
CN Phosphatase, triphosphoinositide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 37205-54-2 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 4- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 37288-19-0 HCAPLUS
CN Phosphodiesterase, monophosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 104645-76-3 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 124248-47-1 HCAPLUS
CN Phosphatase, phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:674777 HCAPLUS
DOCUMENT NUMBER: 137:210986
TITLE: Methods of identifying agents affecting atrophy and hypertrophy
INVENTOR(S): Glass, David J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002123456	A1	20020905	US 2002-86201	20020228
WO 2002069890	A2	20020912	WO 2002-US5876	20020228
WO 2002069890	A3	20021107		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-273174P P 20010302

AB The present invention provides a method for inhibiting atrophy or causing hypertrophy in muscle cells, by inhibiting the action of the phosphatase SHIP2. It further provides a method for inhibiting skeletal muscle atrophy or causing skeletal muscle hypertrophy in vertebrate animals, by inhibiting the Akt pathway through the inhibition of SHIP2. It also provides a method of identifying agents that may be used for inhibiting atrophy or causing hypertrophy in muscle cells, by screening for inhibitors of SHIP2 or inhibitors of the SHIP2 signaling pathway.

IC ICM A61K031-00
ICS G01N033-53; G01N033-567

NCL 514001000

CC 1-12 (Pharmacology)
Section cross-reference(s): 3

IT AIDS (disease)
Aging, animal
Diabetes mellitus
Immobilization
Muscle, disease
Muscular dystrophy
Neoplasm
Starvation, animal
(atrophy induction by; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT **Immobilization**
(bed rest, atrophy induction by; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT **Immunoassay**
(immunoblotting; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT **Immunoassay**
(immunohistochem.; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT Cameras
Cat (Felis catus)
Cattle
Chicken (Gallus domesticus)
Dog (Canis familiaris)
Drug screening

Fluorescence
Gamma ray detectors
Gel electrophoresis
Horse (Equus caballus)
Human
Northern blot hybridization
PCR (polymerase chain reaction)
Phage display
Primates
Rabbit
Rodentia
Scintillation detectors
Sheep
Signal transduction, biological
Swine
Vertebrata
X-ray detectors
(methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT Cameras
(**scintillation**; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT Nucleic acid hybridization
(yeast-two hybrid **assay**; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT **115926-52-8**, Phosphatidylinositol-3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activation of; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

IT **115926-52-8**, Phosphatidylinositol-3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activation of; methods of identifying agents affecting atrophy and hypertrophy in skeletal muscle by screening for inhibitors of SHIP2 phosphatase or its signaling pathway)

RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:539817 HCAPLUS
DOCUMENT NUMBER: 137:90191
TITLE: Identification, cloning, characterization and therapeutic use of a human phosphatidylinositol 4-phosphate 5-kinase family member 56634
INVENTOR(S): Meyers, Rachel A.; Rudolph-Owen, Laura A.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002055682 A2 20020718 WO 2001-US47782 20011113
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002164750 A1 20021107 US 2001-12055 20011113
PRIORITY APPLN. INFO.: US 2000-248325P P 20001114

AB The invention provides isolated nucleic acids mols., designated 56634 nucleic acid mols., which encode novel phosphatidylinositol 4-phosphate 5-kinase members. The cDNA sequence and the encoded amino acid sequence of a human phosphatidylinositol 4-phosphate 5-kinase homolog 56634 (clone Fbh56634FL) are disclosed. Tissue-specific expression profiles, and structural motifs of the polypeptide are provided. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. 56634 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 56634 gene has been introduced or disrupted. The invention still further provides isolated 56634 proteins, fusion proteins, antigenic peptides and anti-56634 antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

IC ICM C12N009-00

CC 7-5 (Enzymes)
Section cross-reference(s): 1, 3, 13, 63

IT Antitumor agents
Drug screening
Gene therapy
Human
Immunoassay
Immunotherapy
Molecular cloning
Nucleic acid hybridization
Protein motifs
Protein sequences
Test **kits**
cDNA sequences
(identification, cloning, characterization and therapeutic use of human phosphatidylinositol 4-phosphate 5-kinase family member 56634)

IT **104645-76-3P**, Phosphatidylinositol 4-phosphate 5-kinase
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(identification, cloning, characterization and therapeutic use of human phosphatidylinositol 4-phosphate 5-kinase family member 56634)

IT **104645-76-3P**, Phosphatidylinositol 4-phosphate 5-kinase
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(identification, cloning, characterization and therapeutic use of human phosphatidylinositol 4-phosphate 5-kinase family member 56634)

RN 104645-76-3 HCAPLUS

CN Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:521952 HCAPLUS
DOCUMENT NUMBER: 137:74468
TITLE: Human phosphatidylinositol-4-phosphate 5-kinase and cDNA and drug screening targeted to regulation and other therapeutic application for related diseases
INVENTOR(S): Zhu, Zhimin
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053714	A2	20020711	WO 2001-EP15321	20011227
WO 2002053714	A3	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-259217P P 20010103
US 2001-331474P P 20011116

AB A human phosphatidylinositol-4-phosphate 5-kinase and cDNA and sequence homologs thereof are disclosed. The mRNA expression profile in various human tissues is provided. Methods for expressing and prepg. related products using recombinant cells are described. These recombinant cells, the enzyme, or nucleic acids encoding the enzyme are useful in screening for modulators of the enzymic activity or gene expression. Methods of screening for its modulators and using them for the treatment of various disease and their effectiveness (in vivo testing of compds./target validation) are described. Reagents that regulate human phosphatidylinositol-4-phosphate 5-kinase and reagents which bind to human phosphatidylinositol-4-phosphate 5-kinase gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, cancer, asthma, and COPD.

IC ICM C12N009-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 7, 13, 63
IT Test **kits**
(diagnostic; human phosphatidylinositol-4-phosphate 5-kinase and cDNA and related drug screening)
IT Ligands
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**labeled** and **immobilized**, used in **phosphatidylinositol-4-phosphate** 5-kinase related drug screening; human **phosphatidylinositol-4-phosphate** 5-kinase and cDNA and related drug screening)
IT **104645-76-3P**, Kinase (phosphorylating), phosphatidylinositol

4-phosphate 5-
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human phosphatidylinositol-4-phosphate 5-kinase and cDNA and related drug screening)

IT **104645-76-3P**, Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5-
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human phosphatidylinositol-4-phosphate 5-kinase and cDNA and related drug screening)

RN 104645-76-3 HCAPLUS

CN Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:368663 HCAPLUS
DOCUMENT NUMBER: 136:381454
TITLE: Protein and cDNA sequences of a novel human phospholipase C sequence homolog and uses thereof
INVENTOR(S): Meyers, Rachel E.; Silos-Santiago, Inmaculada
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038773	A2	20020516	WO 2001-US25252	20010810
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001083321	A5	20020521	AU 2001-83321	20010810
US 2002106774	A1	20020808	US 2001-927112	20010810

PRIORITY APPLN. INFO.: US 2000-246808P P 20001108
WO 2001-US25252 W 20010810

AB The invention provides protein and cDNA sequences of a novel human protein, designated 32544, which has sequence homol. with phospholipase C family members. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. 32544 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 32544 gene has been introduced or disrupted. The invention still further provides isolated 32544 proteins, fusion proteins, antigenic peptides and anti-32544 antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

IC ICM C12N015-54
ICS C12N015-11; C12N009-12; C07K016-40; C12Q001-68; G01N033-50;

A61K038-43; A61K048-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 7, 13
IT Test **kits**
(for detecting phospholipase C sequence homolog 32544; protein and cDNA sequences of novel human phospholipase C sequence homolog and uses thereof)
IT **Immunoassay**
Nucleic acid hybridization
(for detecting the presence of phospholipase C sequence homolog in a sample; protein and cDNA sequences of novel human phospholipase C sequence homolog and uses thereof)
IT **63551-76-8P**, Phospholipase C
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sequence homolog; protein and cDNA sequences of novel human phospholipase C sequence homolog and uses thereof)
IT **63551-76-8P**, Phospholipase C
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sequence homolog; protein and cDNA sequences of novel human phospholipase C sequence homolog and uses thereof)
RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:256482 HCAPLUS
DOCUMENT NUMBER: 136:291005
TITLE: Sequences of a human phosphatidylinositol-specific phospholipase C sequence homolog and uses in diagnosis, therapy and drug screening
INVENTOR(S): Zhu, Zhimin
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026996	A2	20020404	WO 2001-EP11012	20010924
WO 2002026996	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002010514	A5	20020408	AU 2002-10514	20010924

PRIORITY APPLN. INFO.: US 2000-235552P P 20000927
WO 2001-EP11012 W 20010924

AB The invention provides protein and cDNA sequences of a novel human phosphatidylinositol-specific phospholipase C sequence homolog fragment. The invention also provides reagents and methods of regulating a human phosphatidylinositol-specific phospholipase C sequence homolog. Reagents which regulate human phosphatidylinositol-specific phospholipase C-like enzyme and reagents which bind to human phosphatidylinositol-specific phospholipase C-like enzyme gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, asthma, cancer, CNS disorders, and chronic obstructive pulmonary disease.

IC ICM C12N015-55
ICS C12N009-18; C12N005-10; C12Q001-68; A61K038-46; C07K019-00; G01N033-53; A61P011-06; A61P035-00; A61P025-00; A61P011-00

CC 7-2 (Enzymes)
Section cross-reference(s): 1, 3, 13

IT Test **kits**
(diagnostic; sequences of human phosphatidylinositol phospholipase C sequence homolog and uses in diagnosis, therapy and drug screening)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**immobilized**, phosphatidylinositol-specific phospholipase C sequence homolog, for drug screening; sequences of human phosphatidylinositol phospholipase C sequence homolog and uses in diagnosis, therapy and drug screening)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**labeled**, **phosphatidylinositol**-specific **phospholipase** C sequence homolog, for drug screening; sequences of human **phosphatidylinositol phospholipase** C sequence homolog and uses in diagnosis, therapy and drug screening)

IT **63551-76-8**, Phosphatidylinositol-specific phospholipase C
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequence homolog; sequences of human phosphatidylinositol phospholipase C sequence homolog and uses in diagnosis, therapy and drug screening)

IT **63551-76-8**, Phosphatidylinositol-specific phospholipase C
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequence homolog; sequences of human phosphatidylinositol phospholipase C sequence homolog and uses in diagnosis, therapy and drug screening)

RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:107559 HCAPLUS
DOCUMENT NUMBER: 136:163297
TITLE: Sequences of human phosphatidylinositol phospholipase C-like protein and uses in diagnosis, therapy and drug screening
INVENTOR(S): Kossida, Sophia
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010403	A2	20020207	WO 2001-EP8693	20010727

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-221917P P 20000731
US 2001-280112P P 20010402

AB The invention provides protein and cDNA sequences of human proteins (phosphatidylinositol phospholipase C-like protein), which have sequence homol. with phosphatidylinositol phospholipase Cs. Reagents which regulate human phosphatidylinositol-specific phospholipase C-like enzyme and reagents which bind to human phosphatidylinositol-specific phospholipase C-like enzyme gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, cancer, peripheral and central nervous system diseases, and chronic obstructive pulmonary disease.

IC ICM C12N015-55
ICS C12N009-16; C12N015-63; C12N005-10; C12Q001-68; G01N033-573

CC 7-2 (Enzymes)
Section cross-reference(s): 1, 3, 13

IT Test **kits**
(diagnostic; sequences of human phosphatidylinositol phospholipase C-like protein and uses in diagnosis, therapy and drug screening)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**immobilized**, phosphatidylinositol phospholipase C-like protein, for drug screening; sequences of human phosphatidylinositol phospholipase C-like protein and uses in diagnosis, therapy and drug screening)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**labeled**, **phosphatidylinositol phospholipase** C-like protein, for drug screening; sequences of human **phosphatidylinositol phospholipase** C-like protein and uses in diagnosis, therapy and drug screening)

IT **63551-76-8**, Phospholipase C, phosphatidylinositol
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-like protein; sequences of human phosphatidylinositol phospholipase C-like protein and uses in diagnosis, therapy and drug screening)

IT **63551-76-8**, Phospholipase C, phosphatidylinositol
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-like protein; sequences of human phosphatidylinositol phospholipase C-like protein and uses in diagnosis, therapy and drug screening)

RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:851435 HCAPLUS
DOCUMENT NUMBER: 136:1570
TITLE: Compositions, **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases associated therewith
INVENTOR(S): Hanrahan, Catherine F.; Feldman, Marc; Trepicchio, William L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001088199	A2	20011122	WO 2001-US16022	20010517
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002039734	A1	20020404	US 2001-860655	20010517
PRIORITY APPLN. INFO.:			US 2000-205204P P	20000518

AB The invention relates to compns., kits and methods for identifying, detecting, and modulating the differentiation, growth, and/or maturation of Th1 or Th2 cells. The invention further relates to compns., kits, and methods for detecting, characterizing, preventing, and treating a Th1- or Th2-assocd. condition. A variety of markers are provided, wherein changes in the levels of expression of one or more of the markers is correlated with the presence of a Th1 or Th2 cell or Th1- or Th2-assocd. condition. Macrophage inhibitory factor (MIF) gene expression which is increased in both Th1-inducing and TH2-inducing condition is analyzed.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 13, 14
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (1-8D Interferon-induced gene, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ABC (ATP-binding cassette) transporters, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Agglutinins and Lectins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Activation-induced, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Genetic element

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Ahnak-Related Sequence, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Amphiphysin, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Arp2/3 protein complex subunit, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BRCA2, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BST-2-bone marrow stromal cell antigen 2, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C/EBP (CCAAT box/enhancer element-binding protein), .gamma., TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT CD antigens
Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD97, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR3, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR4, type 7, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR5, type 7, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DEAD box-contg., cl.1042, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(DNA-binding, leucine zipper-contg., Interferon-induced, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DNA-binding, zinc finger-contg., Rung finger contg., TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DNA-binding, zinc finger-contg., bcI6, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (EP2 subtype, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ERM, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Epstein-Barr virus-induced, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GATA-3, gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GBP (guanylate-binding protein), isoform I, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GBP (guanylate-binding protein), isoform II, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GTP-binding, p78, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Golli-Mbp, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT G proteins (guanine nucleotide-binding proteins)

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G16, G.alpha.16, gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-E, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT High-mobility group proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HMG-I(Y), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSP 70, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IFN consensus sequence binding protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IFN-.gamma. inducible early response gene (INP10), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IFN-.gamma. protein (IP30), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Insulin-like growth factor-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IGFBP-4, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Annexins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(II, gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(INF-responsive, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ISGF-2 (interferon-stimulated gene factor 2), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(Interferon-induced 17Kd/15Kd protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (KCNO1, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study) (KIAA0005, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Orphan receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (L5, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Leukemia virus receptor 2, P transporter, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MAP (microtubule-assocd. protein), echinoderm, homolog of, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class I, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class II, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class II, heavy chain, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MIF (macrophage inhibitory factor), gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and

diseases assocd. therewith)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Metabolic, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (NF-IL3A-basic ZIP protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (NF-.kappa.B (nuclear factor .kappa.B), p65-RelA, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (NRF-1 (nuclear respiratory factor 1), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ninjurin1 nerve injury-induced protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Nuclear domain 10 protein (NDP52), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (OMP (olfactory marker protein), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PQ-rich, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (RGS1 (B cell activation gene regulator of G-protein signalling), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (RTVP-1, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Rb, p107, TH1 and/or TH2 cell differentiation marker; compns.,

kits, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Ribonucleoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ro/SSA homolog, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SMARCA2, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SMARCB1, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (STAT1, gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (STAT4, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAP-1 (transporter in antigen processing 1), gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAP-2 (transporter in antigen processing 2), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TATA box-binding, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TGF-.beta.-stimulated protein TSC-22, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Cord blood
Lymph node
(TH1 and TH2 cell collected from; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TH1 and/or TH2 cell differentiation induction by; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Cell division
(TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT CD2 (antigen)
CD38 (antigen)
Calcitonin receptors
Calreticulin
Clusterin
FSH receptors
Fas antigen
Interleukin 16
Interleukin 1.beta.
Interleukin 4 receptors
Interleukin 8
Keratins
LFA-3 (antigen)
Laminins
Macrophage inflammatory protein 1.alpha.
Macrophage inflammatory protein 1.beta.
Myoglobins
Proteolipid protein
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Cell differentiation
(TH1 or TH2; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TP53, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(UDP-galactose, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Ubiquitin-activating enzyme E1 related, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Phosphoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VASP (vasodilator-stimulated phosphoprotein), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VHL (von Hippel-Lindau), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(WD protein IR10, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(actin-capping, macrophage, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(actin-capping, .alpha., TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Angiotensin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(angiotensin II, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT CD28 (antigen)
CD3 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Genetic markers
(assocd. with TH1 or TH2 cell differentiation; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Disease, animal
(assocd. with TH1 or TH2 cell; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autoantigens, p542, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Amyloid precursor proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding protein to, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(butyrophilins, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Ha-ras1, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calgizzarin, TH1 and/or TH2 cell differentiation marker; compns.,

kits, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT DNA microarray technology
Drug screening
(compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT **Immunoassay**
(enzyme-linked immunosorbent **assay**; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for EMR1, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for RNA polymerase subunit hRPB "33", TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Test **kits**
(for TH1 and TH2 cell detection; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interleukin 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for TH1 and TH2 cell differentiation induction; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for chemokines, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for leukemia inhibitory factor, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for protein 4-1BB, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Immunoglobulins
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments, to TH1 and TH2 cell marker proteins; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Metallothioneins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(from cadmium treated cells, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and

modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene c-crk, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Cyclins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Heat-shock proteins
Interleukin 4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antigen presentation
Cell death
Organelle
(gene involved in, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Protein degradation
(gene invovled in, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Signal transduction, biological
(gene invovled in, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene rab5, interacting protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT T cell (lymphocyte)
(helper cell/inducer, TH1; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT T cell (lymphocyte)
(helper cell/inducer, TH2; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(homeodomain-contg., homolog 2, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inducible, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(interferon IGUP 1-5111 protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 12, .beta.2 chain, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(junB, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Myosins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(light chain, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(light chains, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lymphoid-specific, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(macrophage inflammatory protein 3.alpha., IFN-inducible, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(membrane, hematopoietic, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Kinesins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mitotic centromere-assocd., TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Diagnosis
(mol.; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT CD4-positive T cell
(naive, TH1 and TH2 cell differentiated from; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nexins, Glia-Derived, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of Rhesus (Rh) Blood Group System, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT cDNA
mRNA
RL: ANT (Analyte); ANST (Analytical study)
(of TH1 and TH2 cell marker genes; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Repetitive DNA sequences
(of pTR2 mRNA, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of retrovirus, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene, c-src-1, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p84 (clone N5-4), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phospholipid-transporting, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pre-B-cell leukemia transcription factor 2, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interleukin 13
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(precursor, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Cell nucleus
Chromatin
(protein assocd. with, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Bloom's syndrome
(protein responsible for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interleukin 12
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(recombinant, TH1 and/or TH2 cell differentiation induction by; compns., **kits**, and methods for identification and modulation

of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(restin, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(secretory, Epididymal and tissue specific, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Ribonucleoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(small nuclear RNA-contg., autoantigen, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tactile protein, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymus and activation regulated, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(to CD28, for TH1 and TH2 cell differentiation induction; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(to CD3, for TH1 and TH2 cell differentiation induction; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(to IL-12, TH1 and/or TH2 cell differentiation induction by; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to TH1 and TH2 cell marker proteins; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 7, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tyrosine-contg., SLP-76, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation

of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ubiquitin-conjugating, Ubch5, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.2-macroglobulin, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.6, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.beta. chemokine receptor CCR7, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.beta.-, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.gamma., gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9025-82-5, Phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (4B, TH1 and/or TH2 cell differentiation marker, 6B, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9001-16-5, Cytochrome oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (4B, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 372092-80-3, Protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CDC-2 like, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9047-64-7, Ribonucleotide reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (M1 subunit, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 139691-92-2, Serine protease inhibitor
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Placental bikunin, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9035-51-2, Cytochrome P 450, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TH1 and/or TH2 cell differentiation marker, dioxin-inducible, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 1553-55-5, 3-Hydroxy-3-methylglutaryl coenzyme A 9004-06-2, Elastase 9013-93-8, Phospholipase 9014-24-8 9023-58-9, Argininosuccinate synthetase 9023-62-5, Glutathione synthetase 9023-66-9, Formyltetrahydrofolate synthetase 9027-97-8, Methenyltetrahydrofolate cyclohydrolase 9029-14-5, Methylenetetrahydrofolatedehydrogenase 9029-66-7, Steroid 11.beta.-hydroxylase 9030-22-2, Uridine phosphorylase 9030-45-9, Glutamine : fructose-6-phosphate amidotransferase 9037-14-3, Synthase, aminolevulinate 37205-49-5, Methylmalonate semialdehyde dehydrogenase 37237-44-8, Ceramide glucosyltransferase 73361-25-8 78689-77-7, Fructose 6-phosphate,2-kinase 150605-50-8, MAP kinase phosphatase 182762-08-9, Caspase 4 289899-93-0, JNK2 361186-44-9, Protein phosphatase 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9025-75-6, Phosphoprotein phosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(catalytic subunit (PPP3CA), Calmodulin-dependen, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9023-56-7, CTP synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dioxin-inducible, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 37205-63-3, ATP synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9023-64-7, .gamma.-Glutamylcysteine synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(light subunit, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9001-84-7, Phospholipase A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lysosomal type Ca2+-independent, gene KIAA0106, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 9027-13-8, Enoyl-CoA hydratase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mitochobdrial, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 79747-53-8, Tyrosine phosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(non-receptor protein, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(subunit, TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT **104645-76-3**, Phosphatidylinositol-4- phosphate 5-kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha., type I (68kDa), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.delta. type, as TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

IT **104645-76-3**, Phosphatidylinositol-4- phosphate 5-kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha., type I (68kDa), TH1 and/or TH2 cell differentiation marker; compns., **kits**, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases assocd. therewith)

RN 104645-76-3 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 4-phosphate 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:545896 HCAPLUS
DOCUMENT NUMBER: 135:133154
TITLE: Sixty-six prostate cancer associated genes and their products
INVENTOR(S): Rees, Robert Charles; Li, Geng; Mian, Shahid
PATENT ASSIGNEE(S): The Nottingham Trent University, UK
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053524	A2	20010726	WO 2001-GB188	20010118
WO 2001053524	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1250457	A2	20021023	EP 2001-901262	20010118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-993 A 20000118
WO 2001-GB188 W 20010118

AB The application discloses cancer-assocd. genes and their products, esp. those identifiable by serol. identification of antigens by recombinant expression cloning (SEREX). The genes and products are used to identify, track and treat cancer. Preferably the cancer is prostate cancer. CDNA

expression libraries were constructed from prostate cancer tissues and the inserted cDNA was evaluated by restriction mapping. The invention also disclosed mutations identified in a few of the cloned cancer-assocd. genes.

IC ICM C12Q001-68
ICS G01N033-574; A61K048-00; A61K039-00; A61K039-395; C07H021-04; C12N015-63; C07K014-47

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 7, 14, 15

IT **Immunoassay**
(enzyme-linked immunosorbent **assay**; sixty-six prostate cancer assocd. genes and their products)

IT Antitumor agents
Genetic vectors
Nucleic acid hybridization
Test **kits**
Tumor markers
Vaccines
cDNA sequences
(sixty-six prostate cancer assocd. genes and their products)

IT **63551-76-8**
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.gamma.1; sixty-six prostate cancer assocd. genes and their products)

IT **63551-76-8**
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.gamma.1; sixty-six prostate cancer assocd. genes and their products)

RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:310180 HCAPLUS
DOCUMENT NUMBER: 133:173735
TITLE: Measurement of phosphoinositide 3-kinase activity
AUTHOR(S): Ward, Stephen G.
CORPORATE SOURCE: Head of Pharmacology, University of Bat, Bath, UK
SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (2000), 138(Chemokine Protocols), 163-172
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two methods to measure phosphoinositide 3-kinase (PI 3-kinase) were described. The transfer of .gamma.-phosphate of ATP to the D-3 position of the inositol head group of phosphoinositide lipids was detd. The 1st method relied on metabolic labeling of intact cellular pools of ATP with [32P]Pi followed by lipid extn. and sepn. of the phosphorylated lipids by HPLC. The 2nd procedure used distinct substrates such as phosphatidylinositol under in vitro assay conditions. Advantages and disadvantages of the methods were characterized.

CC 7-1 (Enzymes)

IT **Phosphatidylinositols**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(3-**phosphate**, **labeled** with [32P]; metabolic **labeling** of intact cellular pools of ATP with [32P] **phosphatidylinositol** followed by lipid extn. and HPLC)

IT **Immunoassay**
(immunopptn.; phosphoinositide 3-kinase activity measured by immunopptn. with distinct substrates)

IT **Phosphatidylinositol** 3,4,5-trisphosphate
Phosphatidylinositol 3,4-bisphosphate
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**labeled** with [32P]; metabolic **labeling** of intact cellular pools of ATP with [32P] **phosphatidylinositol** followed by lipid extn. and HPLC)

IT Extraction
HPLC
(metabolic **labeling** of intact cellular pools of ATP with [32P] **phosphatidylinositol** followed by lipid extn. and HPLC)

IT **115926-52-8**, Phosphoinositide 3-kinase
RL: ANT (Analyte); ANST (Analytical study)
(measurement of phosphoinositide 3-kinase activity by detection of D-3 phosphoinositide lipids)

IT 56-65-5, ATP, biological studies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(metabolic **labeling** of intact cellular pools of ATP with [32P] **phosphatidylinositol** followed by lipid extn. and HPLC)

IT **115926-52-8**, Phosphoinositide 3-kinase
RL: ANT (Analyte); ANST (Analytical study)
(measurement of phosphoinositide 3-kinase activity by detection of D-3 phosphoinositide lipids)

RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:144575 HCAPLUS
DOCUMENT NUMBER: 132:193262
TITLE: Enhanced phosphorylation of p53 by ATM in response to DNA damage
INVENTOR(S): Shiloh, Yosef; Smorodinsky, Nehama I.
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development, Israel
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 982318	A2	20000301	EP 1999-306775	19990826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9944730	A1	20000309	AU 1999-44730	19990825

JP 2000256400 A2 20000919 JP 1999-281877 19990826
PRIORITY APPLN. INFO.: US 1998-97898P P 19980826
AB Antibodies directed against the ATM protein and peptide derivs. of the protein are provided. Also provided is a diagnostic tool for detg. the presence of A-T having a detector for detecting ATM protein levels and quantification tools for analyzing the ATM protein levels. A kit for detecting the presence of A-T contg. a detector for detecting ATM protein levels and a quantifier for analyzing ATM protein levels are also provided.
IC ICM C07K016-40
ICS G01N033-573; C12Q001-48
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 14
IT Test **kits**
(diagnostic; enhanced phosphorylation of p53 by ATM in response to DNA damage)
IT **Immunoassay**
(immunopptn.; enhanced phosphorylation of p53 by ATM in response to DNA damage)
IT **115926-52-8**, Phosphatidylinositol-3 kinase 182970-53-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhanced phosphorylation of p53 by ATM in response to DNA damage)
IT **115926-52-8**, Phosphatidylinositol-3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhanced phosphorylation of p53 by ATM in response to DNA damage)
RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:691212 HCAPLUS
DOCUMENT NUMBER: 131:319324
TITLE: Cloning of human SH2 domain-containing proteins and their diagnostic and therapeutic applications
INVENTOR(S): Stewart, Timothy A.; Lu, Yanmei
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 104
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954467	A1	19991028	WO 1999-US8847	19990423
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324297	AA	19991028	CA 1999-2324297	19990423
AU 9937570	A1	19991108	AU 1999-37570	19990423
AU 741133	B2	20011122		
EP 1071773	A1	20010131	EP 1999-919975	19990423

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002512032	T2	20020423	JP 2000-544799	19990423
US 6326482	B1	20011204	US 1999-367206	19990809
US 6472585	B1	20021029	US 2000-648183	20000825
US 2002058309	A1	20020516	US 2001-866028	20010525
US 2002102622	A1	20020801	US 2001-901540	20010709
US 2002146707	A1	20021010	US 2001-901257	20010709
US 2002147322	A1	20021010	US 2001-931087	20010815
WO 2002101069	A2	20021219	WO 2002-US10513	20020403

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1998-82767P	P	19980423
US 1998-113296P	P	19981222
US 1994-233609	A2	19940425
US 1994-286304	A3	19940805
US 1995-443129	A1	19950517
US 1996-733850	B1	19961018
US 1997-67411P	P	19971203
US 1997-69278P	P	19971211
US 1997-69334P	P	19971211
US 1997-69335P	P	19971211
US 1997-69425P	P	19971212
US 1997-69694P	P	19971216
US 1997-69696P	P	19971216
US 1997-69702P	P	19971216
US 1997-69870P	P	19971217
US 1997-69873P	P	19971217
US 1997-68017P	P	19971218
US 1998-70440P	P	19980105
US 1998-74086P	P	19980209
US 1998-74092P	P	19980209
US 1998-75945P	P	19980225
US 1998-33114	B1	19980302
US 1998-112850P	P	19981216
US 1998-216021	B1	19981216
US 1998-218517	B1	19981222
US 1999-234730	B1	19990121
US 1999-254311	A1	19990303
WO 1999-US8847	W	19990423
US 1999-367206	A3	19990809
US 2000-648252	B1	20000825
US 2000-648258	B1	20000825
US 2001-880457	A	20010612

AB The present invention relates to nucleotide sequences, including expressed sequence tags (ESTs), oligonucleotide probes, polypeptides, antagonists and agonists vectors and host cells expressing, and immunoadhesins and antibodies to PRO201, PRO308 or PRO309 polypeptides. The invention further relates to compns. and method for the diagnosis and treatment of neoplastic cell growth and proliferation in mammals, including humans. The invention is based in part on the identification of genes that are amplified in the genome of tumor cells. Such gene amplification is expected to be assocd. with the overexpression of the gene product and

contribute to tumorigenesis. Accordingly, the proteins encoded by the amplified genes are believed to be useful targets for the diagnosis and/or treatment (including prevention) of certain tumors (e.g. cancer) and may act as predictors of the prognosis of tumor treatment.

IC ICM C12N015-12
ICS C07K014-47; G01N033-53; C12Q001-68; C12N015-62; C12N015-11; C07K016-18

CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 13, 63

IT Antitumor agents
Apoptosis
Immunoassay
Molecular cloning
Transformation, neoplastic
(cloning of human SH2 domain-contg. proteins and their diagnostic and therapeutic applications)

IT Test **kits**
(diagnostic; cloning of human SH2 domain-contg. proteins and their diagnostic and therapeutic applications)

IT **115926-52-8**, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PRO201/Nsp1 interaction with; cloning of human SH2 domain-contg. proteins and their diagnostic and therapeutic applications)

IT **115926-52-8**, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PRO201/Nsp1 interaction with; cloning of human SH2 domain-contg. proteins and their diagnostic and therapeutic applications)

RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:183922 HCAPLUS
DOCUMENT NUMBER: 130:234341
TITLE: Simple method and **kit** for detecting cancer cells inside abdominal cavity.
INVENTOR(S): Kunieda, Katsuyuki; Sugiyama, Yasuyuki; Umemoto, Takao; Kawai, Masahiko; Kawaguchi, Noritaka; Suhara, Takashi; Saji, Shigetoyo; Tsuji, Yasushi
PATENT ASSIGNEE(S): Gifu University, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11072496	A2	19990316	JP 1997-245990	19970828

PRIORITY APPLN. INFO.: JP 1997-245990 19970828

AB A simple method and kit are described for detecting cancer cells inside abdominal cavity with high precision using a simple carcinoembryonic antigen (CEA) measuring kit. This method can be used to detect stomach cancer upon cytodiagnosis during the surgery of potential peritoneal tumor

even at the clinic without a pathologist. Cell pellets obtained from isotonic sodium chloride soln. used for washing the inside of abdominal cavity of stomach cancer patient are washed with phosphate buffer using centrifugation and resuspended. This cell suspension is treated with ultrasonication, preferably after phosphatidylinositol phospholipase C is added. Cancer cells inside abdominal cavity is detected by measuring the concn. of CEA present in the supernatant after being released from the surface of cancer cells.

IC ICM G01N033-574
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 14
ST stomach cancer cell abdominal cavity diagnosis; carcinoembryonic antigen peritoneal tumor detection **kit**
IT Sonication
(Ultrasonication; simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT Abdomen
(abdominal cavity; simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT Diagnosis
(cancer; simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT Neoplasm
(diagnosis; simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT Filters
(microfiber, glass; simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT **Immunoassay**
Peritoneum
Stomach, neoplasm
Test **kits**
(simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT Carcinoembryonic antigen
RL: ANT (Analyte); ANST (Analytical study)
(simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT **63551-76-8**, Phospholipase C, phosphatidylinositol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(simple method and **kit** for detecting cancer cells inside abdominal cavity)
IT **63551-76-8**, Phospholipase C, phosphatidylinositol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(simple method and **kit** for detecting cancer cells inside abdominal cavity)
RN 63551-76-8 HCAPLUS
CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:374652 HCAPLUS
DOCUMENT NUMBER: 129:146513
TITLE: **Phosphoinositidase** C activation **assay**. I. Cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]

phosphoinositols
AUTHOR(S): Bird, Ian M.
CORPORATE SOURCE: Department of OB/Gyn, University of Wisconsin at Madison, Madison, WI, USA
SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (1998), 105(Phospholipid Signaling Protocols), 1-9
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Methods are outlined for the cellular labeling and extn. of phosphoinositides and phosphoinositols.
CC 9-8 (Biochemical Methods)
Section cross-reference(s): 6, 7
ST **phosphoinositol phosphoinositide label phosphoinositidase** C
IT Exchange reaction
(cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]**phosphoinositols**)
IT **Phosphoinositides**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]**phosphoinositols**)
IT 68247-19-8P, Inositol **phosphate**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]**phosphoinositols**)
IT **37213-51-7, Phosphoinositidase** C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]**phosphoinositols**)
IT **37213-51-7, Phosphoinositidase** C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cell **labeling**, stimulation, and recovery of cellular [3H] **phosphoinositides** and [3H]**phosphoinositols**)
RN 37213-51-7 HCAPLUS

L31 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:805885 HCAPLUS
DOCUMENT NUMBER: 128:47305
TITLE: Regulation of cytokine production in a hematopoietic cell
INVENTOR(S): Gelfand, Erwin W.; Johnson, Gary L.
PATENT ASSIGNEE(S): National Jewish Medical and Research Center, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9745736	A1	19971204	WO 1997-US9102	19970530
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5910417	A	19990608	US 1996-656563	19960531
AU 9735672	A1	19980105	AU 1997-35672	19970530
US 6495331	B1	20021217	US 1999-305720	19990505

PRIORITY APPLN. INFO.: US 1996-656563 A 19960531
WO 1997-US9102 W 19970530

AB A method useful for regulating cytokine prodn. by a hematopoietic cell by regulating an MEKK/JNKK-contingent signal transduction pathway in such a cell is disclosed. Methods of identifying compds. capable of specifically regulating an MEKK/JNKK-contingent signal transduction pathway in hematopoietic cells, a kit for identifying cytokine regulators, methods to treat diseases involving cytokine prodn., and cells useful in such methods are also described.

IC ICM G01N033-53
ICS C12N005-00; A61K038-00; A61K045-05; A01N037-18

CC 15-5 (Immunochemistry)

IT Gene, animal
Promoter (genetic element)
c-**Kit** (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **Immunoassay**
(enzyme-linked immunosorbent **assay**; control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **Immunoassay**
(fluorescence; control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **Immunoassay**
(immunoblotting; control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **Immunoassay**
(radioimmunoassay; control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **115926-52-8**, Phosphatidylinositol 3-kinase 165245-96-5, p38 MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

IT **115926-52-8**, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(control of cytokine prodn. in hematopoietic cells via regulation of MEK kinase/JNK kinase signal transduction pathway)

RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:757020 HCAPLUS
DOCUMENT NUMBER: 128:30376
TITLE: Identification of members of combinatorial libraries by mass spectrometry
INVENTOR(S): Wennogle, Lawrence Paul; Kelly, Michele Ann; Liang, Hongbin; Goeller, Christine; Thoma, Hans Mathis
PATENT ASSIGNEE(S): Novartis AG, Switz.; Wennogle, Lawrence Paul; Kelly, Michele Ann; Liang, Hongbin; Goeller, Christine; Thoma, Hans Mathis
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743301	A2	19971120	WO 1997-EP2215	19970430
WO 9743301	A3	19980219		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9728890	A1	19971205	AU 1997-28890	19970430

PRIORITY APPLN. INFO.: US 1996-17545P P 19960510
WO 1997-EP2215 W 19970430

AB Methods are provided for characterizing the members of a combinatorial library which bind to a domain of interest. The method utilizes affinity selection in combination with mass spectrometry to provide rapid and efficient screening. The method provides information on relative affinities and mol. wts. of affinity-selected compds. The methods find use in analyzing all types of combinatorial libraries. In a preferred embodiment, the methodol. of the invention is designed to exploit the attributes of soln.-phase libraries, affinity selection, and mass spectrom. to study peptides contg. non-natural amino acids that bind to the src homol. 2 (SH2) domain, particularly to the SH2 domain of phosphatidylinositol 3-kinase. The methodol. is designed to rapidly screen for drugs with the potential to block signal transduction processes and has the addnl. advantage of allowing rapid rank-ordering of substrates that bind to SH2 in this system.

IC ICM C07K001-04
CC 1-1 (Pharmacology)
Section cross-reference(s): 9, 21
IT Affinity chromatography
Combinatorial library
Computer application
Computer program
Drug screening
Electrospray ionization mass spectrometry
Immobilization, biochemical
Mass spectrometry

Peptide library
Signal transduction, biological
(combinatorial library member selection with mass spectrometry)
IT **115926-52-8**, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SH2 domain; combinatorial library member selection with mass spectrometry)
IT 58-85-5, **Biotin** 70-18-8, Glutathione, biological studies
9013-20-1, Streptavidin 50812-37-8, Glutathione S-transferase
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(binding partner; combinatorial library member selection with mass spectrometry)
IT 50812-37-8D, Glutathione S-transferase, fusion products with phosphatidylinositol 3-kinase SH2 domain **115926-52-8D**, Phosphatidylinositol 3-kinase, SH2 domain, glutathione S-transferase fusion products
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(combinatorial library member selection with mass spectrometry)
IT **115926-52-8**, Phosphatidylinositol 3-kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SH2 domain; combinatorial library member selection with mass spectrometry)
RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **115926-52-8D**, Phosphatidylinositol 3-kinase, SH2 domain, glutathione S-transferase fusion products
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(combinatorial library member selection with mass spectrometry)
RN 115926-52-8 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 3- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:13404 HCAPLUS
DOCUMENT NUMBER: 98:13404
TITLE: Preparation of selectively **labeled** **phosphatidylinositol** and **assay** of **phosphatidylinositol**-specific **phospholipase** C
AUTHOR(S): Rittenhouse, Susan Erika
CORPORATE SOURCE: Brigham Hosp., Harvard Med. Sch., Boston, MA, USA
SOURCE: Methods in Enzymology (1982), 86(Prostaglandins Arachidonate Metab.), 3-11
CODEN: MENZAU; ISSN: 0076-6879
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A procedure is described for the prepn. of selectively labeled phosphatidylinositol substrate and the utilization of this substrate in assaying phosphatidylinositol-specific phospholipase C obtained from human

platelets. Platelets are a rich source of the sol. form of the enzyme, and homogeneous prepns. of these cells can be obtained with minimal manipulation. The assay employs phosphatidylinositol labeled on myoinositol and is based upon the enzymic conversion of the labeled material from a lipid-sol. form (phosphatidylinositol) to a water-sol. form (myoinositol phosphate), which can be quantitated by liq. scintillation spectrophotometry.

CC 7-1 (Enzymes)

IT **Phosphatidylinositols**
RL: SPN (Synthetic preparation); PREP (Preparation)
(tritium-**labeled**, prepn. of, for **phosphatidylinositol** **phospholipase** C detn. in human platelets)

IT **63551-76-8**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, of human platelets, tritium-**labeled** **phosphatidylinositol** for)

IT **63551-76-8**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, of human platelets, tritium-**labeled** **phosphatidylinositol** for)

RN 63551-76-8 HCAPLUS

CN Phospholipase C, phosphatidylinositol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L35 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:134304 HCAPLUS

DOCUMENT NUMBER: 106:134304

TITLE: **Labeling** of sarcoplasmic reticulum peptides with **32P-phosphate** and fluorescein 5'-isothiocyanate

AUTHOR(S): Georgoussi, Zafiroula; Evangelopoulos, Athanassios; Heilmeyer, Ludwig M. G., Jr.

CORPORATE SOURCE: Natl. Hell. Res. Found., Athens, 116 35, Greece

SOURCE: Biochemical Pharmacology (1986), 35(24), 4571-3
CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Labeling of rabbit muscle sarcoplasmic reticulum membrane proteins was carried out with [.gamma.-32P]ATP and protein kinase, as well as with FITC. Evidently, the .alpha. and .beta. subunits of phosphorylase kinase are assocd. with the sarcoplasmic reticulum membranes. Since phosphorylase kinase exhibits phosphatidylinositol kinase activity, it is possible that the phosphatidylinositol kinase activity known to be present in these membranes can be attributed to the phosphorylase kinase protein.

CC 7-8 (Enzymes)
Section cross-reference(s): 6, 13

IT **37205-54-2**, Phosphatidylinositol kinase
RL: BIOL (Biological study)
(of sarcoplasmic reticulum membranes, phosphorylase kinase in relation to)

IT **37205-54-2**, Phosphatidylinositol kinase
RL: BIOL (Biological study)
(of sarcoplasmic reticulum membranes, phosphorylase kinase in relation to)

RN 37205-54-2 HCAPLUS

CN Kinase (phosphorylating), phosphatidylinositol 4- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L35 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:537561 HCAPLUS
DOCUMENT NUMBER: 103:137561
TITLE: Enzymic synthesis and hydrolysis of [**32P**]phosphatidylinositol phosphate
AUTHOR(S): Knowles, Aileen F.; Lawrence, C. Martin
CORPORATE SOURCE: Cancer Cent., Univ. California, San Diego, La Jolla, CA, 92093, USA
SOURCE: Biochemical and Biophysical Research Communications (1985), 129(1), 220-5
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosphatidylinositol kinase activity in plasma membrane prepns. of mouse liver was found to be comparable to that in A431 cells and higher than that in 3 human tumor xenografts. This activity was exploited in prepg. 32P-labeled phosphatidylinositol phosphate of high specific radioactivity in which .apprx.4% of the radioactivity of the substrate, [.gamma.-32P]ATP, was incorporated into the lipid. The subcellular distribution of phosphatidylinositol phosphate phosphatase in a human astrocytoma xenograft was detd. using [32P]phosphatidylinositol phosphate as a substrate. The highest phosphatase activity was found in the plasma membranes.
CC 7-3 (Enzymes)
Section cross-reference(s): 9, 13
IT 98445-12-6
RL: BIOL (Biological study)
(in human astrocytoma cells, subcellular distribution of, **phosphatidylinositol phosphate labeled** with **phosphorus**-32 in detn. of)
IT **37205-54-2**
RL: BIOL (Biological study)
(of cell membrane of liver and neoplasm, phosphorus-32-contg. phosphatidylinositol phosphate prepn. in relation to)
IT **37205-54-2**
RL: BIOL (Biological study)
(of cell membrane of liver and neoplasm, phosphorus-32-contg. phosphatidylinositol phosphate prepn. in relation to)
RN 37205-54-2 HCAPLUS
CN Kinase (phosphorylating), phosphatidylinositol 4- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L35 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:487727 HCAPLUS
DOCUMENT NUMBER: 85:87727
TITLE: Acetylcholine causes an increase in the hydrolysis of triphosphoinositide prelabeled with [**32P**] **phosphate** or [3H]myo-inositol and a corresponding increase in the **labeling** of **phosphatidylinositol** and **phosphatidic** acid in rabbit iris muscle
AUTHOR(S): Abdel-Latif, Ata A.; Akhtar, Rashid A.
CORPORATE SOURCE: Dep. Biochem., Univ. Hosp., Nottingham, UK
SOURCE: Biochemical Society Transactions (1976), 4(2), 317-21
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal

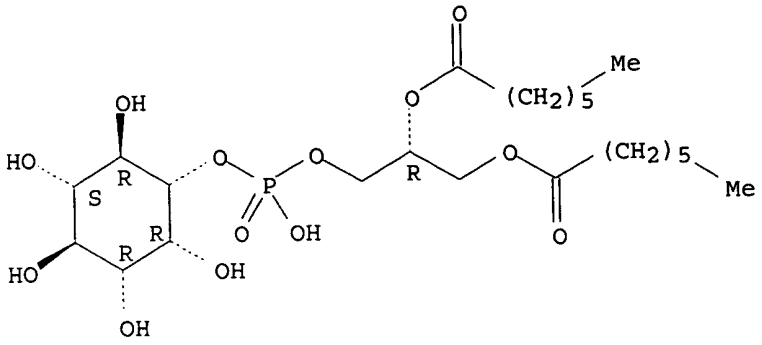
LANGUAGE: English
AB In the iris muscle of the rabbit in vitro, acetylcholine [51-84-3] (.apprx.0.5mM) stimulated hydrolysis of triphosphoinositide, previously labeled in vivo or in vitro with 32PO4 or myo-inositol-3H, to diphosphoinositide, subsequently leading to an increase in phosphatidylinositol and phosphatidic acid. This effect of acetylcholine was blocked by atropine (0.27mM). Acetylcholine probably acted by stimulating triphosphoinositide phosphomonoesterase [**9036-01-5**], and atropine probably inhibited this enzyme.
CC 2-5 (Hormone Pharmacology)
IT **9036-01-5**
RL: PROC (Process)
(of iris muscle, acetylcholine stimulation of)
IT **9036-01-5**
RL: PROC (Process)
(of iris muscle, acetylcholine stimulation of)
RN 9036-01-5 HCAPLUS
CN Phosphatase, triphosphoinositide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:323680 HCAPLUS
DOCUMENT NUMBER: 127:14796
TITLE: Mechanism and structure based inhibitors of phospholipase C enzymes
AUTHOR(S): Roberts, Mary F.; Wu, Yiqin; Zhou, Chun; Geng, Dong; Tan, Cristina
CORPORATE SOURCE: Merkert Chemistry Center, Boston College, Chestnut Hill, MA, 02167, USA
SOURCE: Advances in Enzyme Regulation (1996), 36, 57-71
CODEN: AEZRA2; ISSN: 0065-2571
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors synthesized and characterized a series of specific inhibitors for two classes of phospholipase C, E.C. 3.1.4.11 and E.C. 3.1.4.3. The soln. conformation of the lipophilic inhibitors has been detd. using NMR methodol. and the interaction of one of these compds., a diacylphophoramidocholine, with PC-PLC has been examd. by TRNOE techniques.
CC 7-3 (Enzymes)
IT 9001-86-9, Phospholipase C 37213-51-7, **E.C. 3.1.4.11**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism and structure based inhibitors of phospholipase C enzymes)
IT **148437-42-7P 148553-39-3P 151555-14-5P**
157226-01-2P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(mechanism and structure based inhibitors of phospholipase C enzymes)
IT **148437-42-7P 148553-39-3P 151555-14-5P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(mechanism and structure based inhibitors of phospholipase C enzymes)

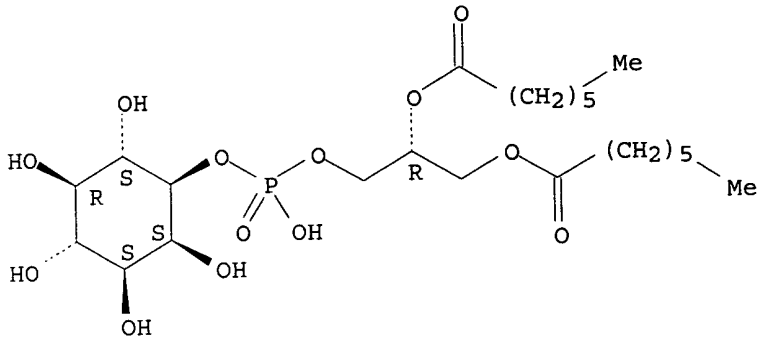
RN 148437-42-7 HCAPLUS
CN D-myo-Inositol, 1-[(2R)-2,3-bis[(1-oxoheptyl)oxy]propyl hydrogen phosphate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



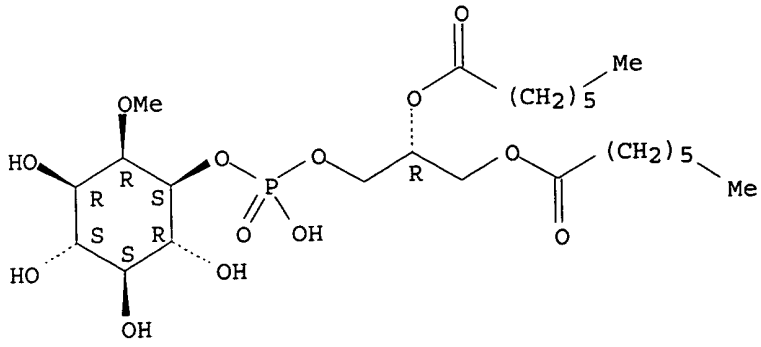
RN 148553-39-3 HCAPLUS
CN D-myo-Inositol, 3-[(2R)-2,3-bis[(1-oxoheptyl)oxy]propyl hydrogen phosphate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 151555-14-5 HCAPLUS
CN D-myo-Inositol, 2-O-methyl-, 1-[(2R)-2,3-bis[(1-oxoheptyl)oxy]propyl hydrogen phosphate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> fil wpids
FILE 'WPIDS' ENTERED AT 10:30:27 ON 09 JAN 2003
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MOST RECENT DERWENT UPDATE:     200301        <200301/DW>
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>>> DUE TO TECHNICAL ISSUES THE UPDATE 200301 HAD INITIALLY BEEN
    INCOMPLETELY LOADED FOR CHEMICAL AND POLYMER CODING DATA.
    THIS HAS BEEN CORRECTED AND THE SDI WILL BE RERUN.
    POSSIBLE DUPLICATE SHIPPINGS OF SDIS WILL NOT BE
    CHARGED FOR. WE APOLOGIZE FOR ANY INCONVENIENCE CAUSED <<<

=> d his

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L1           774 S  ?PHOSPH!TIDYLINOSITOL OR PHOSPHOINOSIT? OR PHOSPHOT INOSIT?
L2           122 S L1 (3A) (KINASE# OR PHOSPHATASE#)
L3           390 S ?PHOSPHO? (2W) KINASE# OR ?PHOSPHO? INOSITOL KINASE#
L4            34 S L1 (3A) ?PHOSPHOLIPASE C
L5             1 S  L1 (3A) (?PHOSPHODIESTERASE?)
L6             0 S L1 (3A) ?PHOSPHOTASE?
L7             6 S L1 (3A) ?PHOSPHATASE?
L8          1129 S L1-L7
L9            29 S (EC OR E C ) (W) (3 1 4 OR 3 1 3 OR 2 7 1)
L10         1157 S L8 OR L9
L11        35662 S ?ASSAY? OR IMMUNOCHEMICAL?
L12          176 S L10 AND L11
L13          483 S 32 P OR 32P
L14          211 S LABEL? (3A) (P OR PHOSPHORUS?)
L15          653 S L13 OR L14
L16            6 S L12 AND L15
L17          161 S ALDEHYDE? (5A) SUPPORT?
L18         9040 S PHOSPHOIMAG? OR SCINTILL? OR AVIDIN# OR STREPAVIDIN? OR BIOTI
L19           10 S L18 AND L12
L20          221 S ?PHOSPHORYLA? (5A) SUBSTRAT?
L21           11 S L12 AND L20
L22         1142 S BIND? (2W) MATRI? OR PHOSPHO IMAG? OR LABEL? (3A) PHOSPH?
L23            8 S L22 AND L12
L24           22 S L16 OR L19 OR L21 OR L23

     FILE 'WPIDS' ENTERED AT 10:30:27 ON 09 JAN 2003
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=> d que l24
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                PHOSPHOINOSIT? OR PHOSPHOT INOSIT? OR ?PHOSPH!TID? INOSITOL?
L2          122 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) (KINASE# OR PHOSPHATASE#
                )
L3          390 SEA FILE=WPIDS ABB=ON  PLU=ON  ?PHOSPHO? (2W) KINASE# OR
                ?PHOSPHO? INOSITOL KINASE#
L4           34 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) ?PHOSPHOLIPASE C
L5            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) (?PHOSPHODIESTERASE?)
L6            0 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) ?PHOSPHOTASE?
L7            6 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) ?PHOSPHATASE?
L8         1129 SEA FILE=WPIDS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5 OR
                L6 OR L7)
L9           29 SEA FILE=WPIDS ABB=ON  PLU=ON  (EC OR E C ) (W) (3 1 4 OR 3 1
                3 OR 2 7 1)
L10        1157 SEA FILE=WPIDS ABB=ON  PLU=ON  L8 OR L9
L11       35662 SEA FILE=WPIDS ABB=ON  PLU=ON  ?ASSAY? OR IMMUNOCHEMICAL?
L12         176 SEA FILE=WPIDS ABB=ON  PLU=ON  L10 AND L11
L13         483 SEA FILE=WPIDS ABB=ON  PLU=ON  32 P OR 32P
L14         211 SEA FILE=WPIDS ABB=ON  PLU=ON  LABEL? (3A) (P OR PHOSPHORUS?)
L15         653 SEA FILE=WPIDS ABB=ON  PLU=ON  L13 OR L14
L16           6 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L15
L18        9040 SEA FILE=WPIDS ABB=ON  PLU=ON  PHOSPHOIMAG? OR SCINTILL? OR
                AVIDIN# OR STREPAVIDIN? OR BIOTIN?
L19          10 SEA FILE=WPIDS ABB=ON  PLU=ON  L18 AND L12
L20         221 SEA FILE=WPIDS ABB=ON  PLU=ON  ?PHOSPHORYLA? (5A) SUBSTRAT?
L21          11 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L20
L22        1142 SEA FILE=WPIDS ABB=ON  PLU=ON  BIND? (2W) MATRI? OR PHOSPHO
                IMAG? OR LABEL? (3A) PHOSPH?
L23           8 SEA FILE=WPIDS ABB=ON  PLU=ON  L22 AND L12
L24          22 SEA FILE=WPIDS ABB=ON  PLU=ON  L16 OR L19 OR L21 OR L23


=> d .wp 1-22

L24  ANSWER 1 OF 22  WPIDS (C) 2003 THOMSON DERWENT
AN   2002-471141 [50]    WPIDS                          same family
DNC  C2002-133876
TI   Assay for lipid kinase or phospholipid phosphatase enzymes
     comprises determining the presence and/or amount of phosphorylated
     or dephosphorylated substrate on binding
     matrix.
DC   B04 B05 D16
IN   GOUELI, S; KARASSINA, N; VIDUGIRIENE, J
PA   (PROM-N) PROMEGA CORP; (GOUE-I) GOUELI S; (KARA-I) KARASSINA N; (VIDU-I)
     VIDUGIRIENE J
CYC  95
PI   WO 2001092560 A2 20011206 (200250)* EN   53p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
            SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001065231 A  20011211 (200250)
     US 2002028477 A1 20020307 (200250)
ADT  WO 2001092560 A2 WO 2001-US17554 20010531; AU 2001065231 A AU 2001-65231
     20010531; US 2002028477 A1 Provisional US 2000-208405P 20000531, US
     2001-871424 20010531
FDT  AU 2001065231 A Based on WO 200192560
```

PRAI US 2000-208405P 20000531; US 2001-871424 20010531
AB WO 200192560 A UPAB: 20020807
NOVELTY - **Assay** for lipid kinase (**EC 2.**
7.1) or phospholipid phosphatase (**EC 3**
.1.3 or **EC 3.1.4**
) enzymes comprises: either (A) contacting the enzyme with a **substrate** to form a **phosphorylated** or **dephosphorylated** product, immobilizing the product on a **binding matrix** and determining the presence and/or amount of bound product; or (B) immobilizing the substrate on a **binding matrix**, contacting the substrate with the enzyme and determining the presence and/or amount of bound product.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for performing such an **assay**, comprising a container of reaction buffer, a container of enzyme substrate, a **binding matrix** and instructions for use of the kit.

USE - The **assay** is especially useful analyzing cell lysates or organic solutions for the presence of 1-**phosphatidylinositol** 4-**kinase** (**EC 2.7.1.67**), 1-**phosphatidylinositol**-4-phosphate 5-**kinase** (**EC 2.7.1.68**), 1-**phosphatidylinositol** 3-**kinase** (**EC 2.**
7.1.137), phosphatidylglycerophosphatase (**EC** 3.1.3.27), **phosphatidylinositol** **bisphosphatase** (EC3.1.3.36), **phosphatidylinositol** 3-**phosphatase** (**EC 3.1.3.64**), (**EC 3.1.3.67**), 1-**phosphatidylinositol phosphodiesterase** (**EC** 3.1.4.10) or 1-**phosphatidylinositol** -4,5-bisphosphate **phosphodiesterase** (**EC 3.**
1.4.11).

ADVANTAGE - The **assay** can be performed quickly and conveniently, directly on tissue or cell extracts, without the need for lipid extraction, and is suitable for use in automated high-throughput **assay** systems.

Dwg.0/11

TECH UPTX: 20020807
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Substrate: This is a **phosphoinositide** of formula (I).
R = 2-24C alkyl, alkenyl, alkanoyl or alkenoyl; and
R2-R6 = H or phosphate.
Provided that R2-R6 are not all phosphate when the enzyme is a kinase and not all H when the enzyme is a phosphatase.

TECHNOLOGY FOCUS - POLYMERS - Preferred Matrix: The **binding matrix** is an aldehyde-activated cellulose support.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - The substrate can include a binding molecule specific for a ligand on the **binding matrix**, especially where the binding molecule/ligand couple is **biotin** /(strept)**avidin**, antigen/antibody, antibody/antigen or antibody/anti-antibody.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - The bound product is preferably detected by analyzing the matrix for **32P-labeled phosphate** groups, incorporated by reacting the enzyme with the substrate in the presence of **labeled phosphate**, using a **scintillation** counter or **phospho-imager**.

L24 ANSWER 2 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-385619 [42] WPIDS
DNN N2002-301990 DNC C2002-108695
TI Screening for an activator or inhibitor of an unstable, soluble protein, such as Rho-kinase, for treating a cerebrovascular condition e.g. hypertension, comprises using a solid support having the protein bound to an antibody.
DC B04 D16 K08 S03
IN GODA, M; IMANISHI, N; KAWANE, K
PA (SUMU) SUMITOMO PHARM CO LTD; (SUMU) SUMITOMO SEIYAKU KK; (GODA-I) GODA M; (IMAN-I) IMANISHI N; (KAWA-I) KAWANE K
CYC 28
PI EP 1203958 A2 20020508 (200242)* EN 24p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2002077296 A1 20020620 (200244)
JP 2002139493 A 20020517 (200248) 18p
ADT EP 1203958 A2 EP 2001-125427 20011031; US 2002077296 A1 US 2001-985127 20011101; JP 2002139493 A JP 2000-334774 20001101
PRAI JP 2000-334774 20001101
AB EP 1203958 A UPAB: 20020704
NOVELTY - Screening (M1) for an activator or inhibitor of a soluble or potentially soluble protein function comprises using an immobilized antibody against a partial peptide (PP) of the protein to capture the protein onto a solid support, reacting a solution containing a test substance with the support, and measuring the activity of the protein after the reaction.

DETAILED DESCRIPTION - Screening (M1) for an activator or inhibitor of the function of a soluble or potentially soluble protein, comprises:

(a) preparing a partial peptide (PP) comprising a part of the amino acid sequence of the protein having the properties:

(i) PP comprises a sequence characteristic of the protein and distinct from proteins belonging to the same family as the protein;

(ii) the sequence comprises 6 amino acids and is located in a highly hydrophilic region;

(iii) the sequence has a functional group capable of binding to a carrier protein; and

(iv) the protein is not inactivated by the reaction between the protein and an antibody raised using the peptide as an antigen;

(b) preparing an antibody having an affinity of 105/M or less, using PP as an antigen;

(c) preparing a solid support immobilized with an antibody to the antibody (Ig) prepared in (b);

(d) immobilizing Ig on the solid support;

(e) applying a cell or tissue homogenate containing the protein to the solid support to immobilize the protein;

(f) reacting a solution of a test substance with the solid support; and

(g) measuring the activity of the protein after completion of the reaction, to determine the effect of the test substance on the protein function.

INDEPENDENT CLAIMS are also included for the following:

(1) an activator or inhibitor of the protein function obtainable by the new method;

(2) purifying a protein comprising:

(a) steps (a) - (e) of M1; and

(b) releasing and recovering the protein from the solid support; and

(3) a solid support useful for a purification system of a protein or a screening system of a soluble protein or a potentially soluble protein prepared by steps (a) - (d) of M1.

ACTIVITY - Hypotensive; antianginal; anticonvulsant; muscular. No suitable biological data is given.

MECHANISM OF ACTION - Phosphorylation inhibitor; **phosphorylation** activator; Rho-**kinase** activator; Rho-kinase inhibitor.

USE - The method is used to screen for an inhibitor or activator of a unstable, soluble or potentially soluble protein, preferably Rho-kinase. The inhibitor is used to inhibit phosphorylation and smooth muscle contraction. It is used to treat hypertension, cardiac angina, or cerebrovascular spasm. The activator is used to promote phosphorylation and induce smooth muscle contraction (all claimed).

ADVANTAGE - The method is of high performance, and provides efficient screening of unstable proteins whose activities are difficult to determine in crude extracts of cell or tissue homogenates.

Dwg.0/9

TECH UPTX: 20020704

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Support: The support of (3) is further prepared by step (e) of M1. the support is in the form of a plate. The tissue homogenate is from bovine cerebral gray matter or from rat brain.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The soluble protein or potentially soluble protein is an enzyme, preferable a serine/threonine kinase, especially a bovine, mouse or rat Rho-kinase. PP comprises 20 amino acids (S1) residing at the C-terminal part of Rho-kinase. The function of the protein is determined by incorporation of **32P** or 33P into a substance, which is estimated using radioactivity of the phosphorus or binding activity of an antibody to a **phosphorylated substrate**. The protein function is determined by the effect of the test substance, estimated using:

(i) an SPA (**Scintillation** Proximity **Assay**) method;

(ii) a multiscreen method; or

(iii) a filter-spot method.

The tissue homogenate is from bovine cerebral gray matter. In (2), the protein is preferable unstable, soluble or potentially soluble and is Rho-kinase.

Preferred Protein: The protein is preferably bovine Rho-kinase.

Ile Gln Gln Asn Gln Ser Ile Arg Arg Pro Ser Arg Gln Leu Ala Pro Asn Lys Pro Ser (S1)

L24 ANSWER 3 OF 22 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-171025 [22] WPIDS

DNN N2002-130111 DNC C2002-052769

TI **Assay** for detecting compounds that modulates histidine kinase activity, by contacting compound with kinase and substrate, and monitoring the rate or absolute amount of phosphate transfer by kinase to the substrate.

DC B04 D16 S03

IN GOLDSCHMIDT, R; LOELOFF, M

PA (GOLD-I) GOLDSCHMIDT R; (LOEL-I) LOELOFF M

CYC 1

PI US 2002004214 A1 20020110 (200222)* 17p

ADT US 2002004214 A1 Provisional US 1999-172924P 19991221, US 2000-733731 20001208

PRAI US 1999-172924P 19991221; US 2000-733731 20001208

AB US2002004214 A UPAB: 20020409

NOVELTY - **Assay** for detecting compounds that modulate histidine kinase (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves contacting a compound (C) with HK and HK substrate, isolating HK substrate by affinity capture and detecting a change in kinase activity by monitoring the rate or absolute amount of

phosphate transfer by HK to the substrate in the presence of (C).

DETAILED DESCRIPTION - **Assay** for detecting compounds that modulate histidine kinase (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves:

(a) identifying compounds that modulate EspB histidine kinase enzymatic activity, by admixing a test compound, an EspB histidine kinase fusion protein comprising an EspB histidine kinase catalytic domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with histidine kinase fusion protein and high energy phosphate source, isolating the EspB histidine kinase fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer to the EspB histidine kinase by autophosphorylation in the presence of the compound; or

(b) identifying compounds that modulate histidine kinase enzymatic activity or modulate interaction of the kinase with its cognate response regulator protein, by admixing a test compound, an EspA cognate histidine kinase or its functional derivative, where the kinase has functional histidine kinase activity, an EspA fusion protein comprising an EspA phosphorylation domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with histidine kinase or its derivative, the EspA fusion protein and the high energy phosphate source, isolating the EspA fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer by the kinase to the EspA fusion protein in the presence of the compound.

An INDEPENDENT CLAIM is also included for a histidine kinase fusion protein (I) comprising a protein domain of the espB gene or its functional derivative having functional catalytic activity and a protein or peptide having at least one affinity capture domain.

ACTIVITY - Antibacterial.

No suitable data is given in the source material.

MECHANISM OF ACTION - Modulator of histidine kinase activity (claimed).

USE - The method is useful for detecting modulators of histidine kinase enzyme activity or its interaction with its cognate response regulator protein (claimed). The identified compounds are useful to inhibit growth and kill bacteria that cause infectious disease, while minimizing any potential toxicity.

ADVANTAGE - The method is a robust, sensitive **assay** of simple design that is easily automated and an **assay** that can be easily modified to allow different histidine kinase and response regulator targets to be tested without significant modification to the design.

Dwg.0/6

TECH UPTX: 20020409

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method is conducted in a single **scintillant** - impregnated or coated vessel. The **phosphorylated** EspB histidine **kinase** or the EspA fusion protein is isolated by affinity capture onto the surface of the vessel.

Preferred Protein: The affinity capture protein or peptide is selected from malE gene of Escherichia coli, the glutathione S-transferase encoding gene of Schistosoma japonicum, and hexahistidine. The EspB histidine kinase catalytic domain comprises the carboxy terminal 311 amino acids of the espB gene. The EspA cognate histidine kinase is EspB, its ortholog or a paralog that can transphosphorylate EspA. The protein domain of (I) comprises about the carboxy terminal 397 or 311 amino acids of the espB gene.

L24 ANSWER 4 OF 22 WPIDS (C) 2003 THOMSON DERWENT

AN 2001-390252 [41] WPIDS
DNC C2001-118904
TI Identifying modulators of protein kinase (PK) activity, useful in developing drugs for treating cancer or diabetes, by measuring the ability of the compound to modulate or mimic the interaction of PK with interacting polypeptides.
DC B04 D16
IN ALESSI, D; BIONDI, R
PA (UYDU-N) UNIV DUNDEE
CYC 24
PI WO 2001044497 A2 20010621 (200141)* EN 180p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA JP US
AU 2001021873 A 20010625 (200162)
EP 1234188 A2 20020828 (200264) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
ADT WO 2001044497 A2 WO 2000-GB4598 20001204; AU 2001021873 A AU 2001-21873 20001204; EP 1234188 A2 EP 2000-985454 20001204, WO 2000-GB4598 20001204
FDT AU 2001021873 A Based on WO 200144497; EP 1234188 A2 Based on WO 200144497
PRAI US 1999-168559P 19991202
AB WO 200144497 A UPAB: 20021031
NOVELTY - Identifying a compound that modulates protein kinase activity, comprising measuring the ability of the compound to inhibit, promote or mimic the interaction of a hydrophobic pocket-containing protein kinase with an interacting polypeptide, is new. The interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or comprises the amino acid sequence (I).

DETAILED DESCRIPTION - Identifying a compound that modulates protein kinase activity, comprising measuring the ability of the compound to inhibit, promote or mimic the interaction of a hydrophobic pocket-containing protein kinase with an interacting polypeptide, is new. The interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or comprises the amino acid sequence (I). The protein kinase has a hydrophobic pocket in the position equivalent to the hydrophobic pocket of mouse Protein Kinase A (PKA) that is defined by residues including Lys76, Leu116, Val80 and/or Lys111 of full-length mouse PKA. The amino acid sequence of the interacting polypeptide is as follows: Phe/Tyr-Xaa-Xaa-Phe/Tyr (I).

INDEPENDENT CLAIMS are also included for the following:

(1) a method of selecting or designing a compound that modulates the activity of the hydrophobic pocket-containing protein kinase, comprising using molecular modeling to select or design a compound that is predicted to interact with the hydrophobic pocket containing protein kinase, the three-dimensional (3D) structure of the compound is compared to the 3D structure of the interacting polypeptide or the hydrophobic pocket;

(2) compounds capable of modulating or that modulate the protein kinase activity of the hydrophobic pocket-containing protein kinase, the compounds modulate the **phosphorylation** of a **substrate** having fewer than 400 amino acids, in the absence of a polypeptide which interacts with the hydrophobic pocket of the kinase and/or has the sequence (I);

(3) a compound identified by the novel method is not full length PKA and does not have sequence (II);

(4) a mutated protein kinase, which has before mutation a hydrophobic pocket in the position equivalent to the hydrophobic pocket of mouse PKA that is defined by residues including Lys76, Leu116, Val80 and/or Lys111 of full-length mouse PKA, and where one or more residues defining the hydrophobic pocket of the protein kinase is mutated;

(5) preparations comprising a hydrophobic pocket-containing protein kinase and a second, interacting compound, where the interacting compound

interacts with the hydrophobic pocket of the protein kinase;

(6) methods of phosphorylating:

(a) a substrate polypeptide for the hydrophobic pocket-containing protein kinase using the preparation of (5); or

(b) p70 S6 kinase on the residue equivalent to Thr412 of full length human p70 S6 kinase, where the p70 S6 kinase is exposed to recombinant 3-**phosphoinositide** dependent protein **kinase**-1 (PDK1);

(7) a method of identifying a compound that modulates the activation and/or phosphorylation of p70 S6 kinase on the residue equivalent to Thr412 of full length human p70 S6 kinase by PDK1, where the activation and/or phosphorylation of p70 S6 kinase on the residue equivalent to Thr412 of full length human p70 S6 kinase by PDK1 is measured in the presence of more than one concentration of the compound;

(8) a compound identified or identifiable by the method of (7);

(9) a method of modulating in a cell the protein kinase activity of a hydrophobic pocket-containing protein kinase, where a recombinant interacting polypeptide is expressed in the cell, and where the interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or has amino acid sequence (I);

(10) a polypeptide comprising the amino acid sequence (I), where the polypeptide does not comprise the amino acid sequence (II) or (IIA) and is not full length PKA;

(11) a fusion polypeptide of the polypeptide of (10) that is not full length PKA;

(12) polynucleotides encoding or suitable for expressing (10) or a mutated protein kinase;

(13) host cells comprising the polynucleotide of (12);

(14) a method of making the polypeptide or a mutated protein kinase comprising culturing the host cell of (13) and isolating the polypeptide;

(15) a polypeptide obtainable by the method of (14);

(16) a method of making the preparation comprising the hydrophobic pocket-containing protein kinase; and

(17) kits of parts useful in carrying out the methods above.

Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr (II) Phe/Tyr-Xaa-Xaa-Phe/Tyr-Ser/Thr-Phe/Tyr (IIA)

ACTIVITY - Cystostatic; antidiabetic; vasotropic; cerebroprotective; antifungal.

No biological data is given.

MECHANISM OF ACTION - Protein kinase modulator; gene therapy.

USE - The method is useful in screening **assays** for developing pharmaceutical compounds or drugs. The compound, polypeptide or polynucleotide is useful in medicine, particularly in the manufacture of a medicament for treating a patient in need of modulation of signaling by a hydrophobic pocket-containing protein kinase. Specifically, the patient has cancer or diabetes or is in need of inhibition of apoptosis, e.g. a patient suffering from tissue injury or ischemic injury, including stroke. The compound or composition is also useful for inhibiting the degree or rate of phosphorylation by the protein kinase. The interacting polypeptide or compound is useful in methods of stabilizing a hydrophobic pocket-containing protein kinase, where the protein kinase is exposed to the compound or polypeptide. The kits are useful in carrying out the methods above. (All claimed). The compound may also be used as an antifungal (or other parasitic, pathogenic or potentially parasitic or pathogenic organism) agent.

Dwg.0/22

TECH UPTX: 20010724

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptide: The interacting polypeptide comprises the amino acid sequence (II), where Zaa represents a negatively charged amino acid residue. The polypeptide may also comprise the amino acid sequence: Phe-Xaa-Xaa-Phe (III). The protein kinase is

PDK1. In particular, the protein kinase is serum and glucocorticoid stimulated protein kinase (SGK), PKB, PKA, p70 S6 kinase, p90 RSK, PKCalpha, PKCdelta, PKC zeta or PRK2. The interacting polypeptide is part of the same polypeptide chain as the protein kinase, where the interaction is an intramolecular interaction. The substrate polypeptide comprises a portion that is the interacting polypeptide. Preferably, the protein kinase is PDK1 and the substrate polypeptide comprises a 39 residue amino acid sequence, fully defined in the specification (IV). The substrate portion and the interacting portion are preferably on separate polypeptide chains. The hydrophobic pocket-containing protein kinase is PDK1, the substrate polypeptide comprises or consists of the sequence (V), and the interacting polypeptide comprises or consists of the sequence (VI). The hydrophobic pocket-containing protein kinase is PDK1 and the substrate polypeptide consists of or comprises the amino acid sequence (V) or (VII). LysThrPheCysGlyThrProGluTyrLeuAlaProGluVal (V) GluProArgIleLeuSerGluGluGluGlnGluMetPheArgAspPheAspTyrIleAlaArg-AspTrpCsy (VI) LysThrPheCysGlyThrProGluTyrLeuAlaProGluValArgArg (VII). The protein kinase, before mutation is PDK1, SGK, p70 S6 kinase or PKB. In the mutated protein kinase, the mutated residues are the residues equivalent to residue Lys76, Val80, Lys111 and/or Leu116 of the full-length mouse PKA. The residue at the position equivalent to residue Lys76 of full length mouse PKA is mutated to an Ala, and/or the residue at the position equivalent to Leu116 of full length mouse PKA is mutated to a Ser, Asp or Glu. The polypeptide of (10) comprises or consists essentially of the C-terminal 223 amino acids of full length PKA. The polypeptide comprises non-overlapping interacting and substrate portions, where the interacting portion comprises the amino acid sequence (I) and the substrate portion comprises a consensus sequence for phosphorylation by the hydrophobic pocket-containing protein kinase. The amino acid sequence (I) and the consensus sequence for phosphorylation are separated by 5-100 amino acids. Preferred Compounds: The compound of (2) inhibits the interaction of the protein kinase with an interacting polypeptide, where the interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or comprises the amino acid sequence (I). The compound does not comprise a polypeptide having the amino acid sequence (II) and is not PKA. The compound modulates the rate or degree of **phosphorylation** of a **substrate** polypeptide of the hydrophobic pocket-containing protein kinase by the hydrophobic pocket-containing protein kinase in the absence or presence of an interacting polypeptide, where an interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or comprises the amino acid sequence (I), and where the substrate polypeptide has fewer than 400 amino acids. The interacting polypeptide may be comprised in a separate polypeptide chain to the hydrophobic pocket-containing protein kinase. The compound is not a polypeptide having the amino acid sequence (II) and is not full length PKA. The compound inhibits the protein kinase activity of the protein kinase to a greater extent towards the hydrophobic pocket-dependent substrate than towards the hydrophobic pocket-independent substrate is selected. In particular, the hydrophobic pocket-dependent substrate is SGK, PRK2, S6K1 or PKC zeta, and the hydrophobic pocket-independent substrate is PKB. The preparation may further comprise the substrate polypeptide, but does not comprise all of the components found in a cell in which protein kinase or compound is naturally found. Preferably, the protein kinase is PDK1, the interacting compound is not a polypeptide comprising the amino acid sequence (II). Preferred Method: In identifying a compound that modulates the protein kinase activity of a hydrophobic pocket-containing protein kinase, the effect of the compound on the rate or degree of **phosphorylation** of a **substrate** polypeptide of the hydrophobic pocket-containing protein kinase by the hydrophobic pocket-containing protein kinase in the presence or absence of an interacting polypeptide is determined. A

compound that modulates the rate or degree of phosphorylation is selected, where the interacting polypeptide interacts with the hydrophobic pocket of the protein kinase and/or comprises the sequence (I) and is comprised in a separate polypeptide chain to the hydrophobic pocket-containing protein kinase, and where the substrate polypeptide has fewer than 400 amino acids. The method may comprise:
(a) determining the effect of a test compound on the protein kinase activity of the protein kinase, and/or its mutant; and
(b) selecting a compound capable of modulating the protein kinase activity of the protein kinase to different extents towards:
(i) a substrate that binds to the hydrophobic pocket of the protein kinase (hydrophobic pocket-dependent substrate); and
(ii) a substrate (such as PKB) that does not bind, or binds to a lesser extent than the first substrate (hydrophobic pocket-independent substrate), to the hydrophobic pocket of the protein kinase.
The method may also involve determining the ability of the compound to bind to the protein kinase mutated at a residue defining at least part of the hydrophobic pocket of the protein kinase, e.g. the residue equivalent to lysine 76 of full-length mouse PKA. The method further comprises determining the effect of the compound on the protein kinase activity of, or ability of the compound to bind to, the protein kinase that is not mutated at the residue defining at least part of the hydrophobic pocket of PDK1. The effect of the compound on the rate or degree of **phosphorylation** of a hydrophobic pocket-dependent **substrate** is also determined. A compound is selected that decreases the protein kinase activity of the protein kinase towards a hydrophobic pocket-dependent substrate, and does not affect or increases the protein kinase activity of the protein kinase towards a hydrophobic pocket-independent substrate. The interaction is an interaction of the hydrophobic pocket of the protein kinase with the polypeptide comprising the amino acid sequence (I). The ability of the compound to inhibit, promote or mimic the interaction of the protein kinase with the interacting polypeptide is measured using surface plasmon resonance.
Preferred Cell: The cell contains a recombinant nucleic acid for expressing the hydrophobic pocket-containing protein kinase and a recombinant nucleic acid for expressing a second polypeptide comprising the amino acid sequence (I). The protein kinase is PDK1, and the second polypeptide does not comprise the amino acid sequence (IIA) and is not a 77 residue amino acid PIF sequence, fully defined in the specification.
Preferred Kits: The kit has a hydrophobic pocket-containing protein kinase and a substrate polypeptide, and optionally a separate interacting polypeptide.

L24 ANSWER 5 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-374851 [39] WPIDS
DNC C2001-114581
TI Identifying inhibitors of viral kinases, by adding a cell comprising a nucleic acid encoding a kinase with a **substrate** which when **phosphorylated** by the **kinase** is deleterious for cell in the presence of test compound.
DC B04 D16
IN MARSCHALL, M; METT, H; STAMMINGER, T; STEIN-GERLACH, M
PA (AXXI-N) AXXIMA PHARM AG
CYC 95
PI WO 2001040503 A2 20010607 (200139)* EN 70p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001030070 A 20010612 (200154)
EP 1242616 A2 20020925 (200271) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

ADT WO 2001040503 A2 WO 2000-EP12303 20001206; AU 2001030070 A AU 2001-30070 20001206; EP 1242616 A2 EP 2000-990663 20001206, WO 2000-EP12303 20001206

FDT AU 2001030070 A Based on WO 200140503; EP 1242616 A2 Based on WO 200140503

PRAI EP 1999-124342 19991206

AB WO 200140503 A UPAB: 20010716

NOVELTY - Identifying kinase inhibitors by adding to a target cell comprising a nucleic acid encoding a kinase, a **substrate** capable of being **phosphorylated** by the **kinase**, where the **phosphorylated substrate** is deleterious for target cell and a test compound and determining if test compound is capable of partially inhibiting the deleterious effect of **phosphorylated substrate** or **phosphorylation** of **substrate**.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a reagent kit for the identification of kinase inhibitors comprising a cell containing a nucleic acid encoding a kinase and a **substrate** capable of being **phosphorylated** by the **kinase**.

USE - The method is useful for identifying inhibitors of viral kinases e.g. kinases from herpes simplex, varicello, muromegalo, roseolo, lymphocrypto and rhadino viruses, preferably from human herpesvirus-1 (HSV-1), human varicella zoster virus (VZV-1) or human cytomegalovirus (HCMV). In particular the kinase is HCMV UL97, HSV-1 or -2 UL13, human VZV ORF47, human HHV-6 UL69, human EBV BGLF-4, human HHV-8 ORF36 kinase or kinase homologs. The kit is also useful for identifying kinase inhibitors (claimed).

ADVANTAGE - The **assay** allows for extremely simple determination of the kinase inhibitory activity of substances together with the determination of cytotoxic effects exerted by the same substances.

Dwg.0/12

TECH UPTX: 20010716

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Enzyme: The kinase is heterologous for the target cell. The kinase is a viral kinase and is encoded by the nucleic acid sequence (its hybridizable sequence or a sequence corresponding to it in the scope of degeneracy of genetic code) of 2124, 1554 or 1530 bp given in the specification. The viral kinase has the amino acid sequence of 707, 518 or 510 amino acids defined in the specification.

Preferred Method: The substrate is gancyclovir, acyclovir or famicyclovir. The target cell is a cultured eukaryotic cell, preferably a mammalian cell and the **phosphorylated substrate** is cytotoxic for the target cell. The target has been transformed with a vector or infected by a virus, comprising the kinase encoding nucleic acid. The deleterious effect mediated by the **phosphorylated substrate** is quantitatively determined by determining signals in the culture supernatant and/or in the target cell.

Quantitative measurement is carried out as a high-throughput screening of candidate compounds for kinase-specific therapeutical drugs. Further noncytotoxic test compounds having kinase inhibiting properties and test compounds having kinase inhibiting properties but additionally cytotoxic side effects are distinguished. The effect of a test compound is determined at several different concentrations of the test compound. The method further comprises determining the effect of a test compound on a control cell which comprises a nucleic acid encoding an inactive variant of the kinase.

L24 ANSWER 6 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-266323 [27] WPIDS
DNN N2001-190438 DNC C2001-080714
TI Identifying modulator of kinase or phosphatase activity, involves contacting enzyme and its substrate in presence and absence of the modulator, contacting the substrate with a reporter and comparing its binding.
DC B04 D16 S03
IN FREARSON, J A
PA (CAMB-N) CAMBRIDGE DRUG DISCOVERY LTD
CYC 94
PI WO 2001025477 A2 20010412 (200127)* EN 22p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000075374 A 20010510 (200143)
ADT WO 2001025477 A2 WO 2000-GB3736 20000929; AU 2000075374 A AU 2000-75374 20000929
FDT AU 2000075374 A Based on WO 200125477
PRAI GB 1999-23208 19991001
AB WO 200125477 A UPAB: 20010518
NOVELTY - Identifying (M1) a modulator (I) of kinase or phosphatase activity, involves contacting the enzyme and its substrate (S) in the presence and absence of (I), contacting (S) with a reporter (R) excluding a natural antibody, which binds phosphorylated (S) with higher affinity than unphosphorylated (S), and comparing the binding of (R) to (S) treated in the presence of (I) than in the absence of (I).

DETAILED DESCRIPTION - Identifying a modulator of kinase, preferably serine/threonine kinase activity, involves a screening **assay**, which involves providing a serine/threonine kinase and a **substrate** which can be **phosphorylated** by the **kinase**, contacting the kinase with its substrate in the presence and absence of a candidate modulator of the activity of the kinase under conditions which permit **phosphorylation** of the **substrate** by the kinase, contacting the treated substrate with (R), and comparing binding of (R) to the treated substrate in the presence of (I) with binding of (R) to the treated substrate in the absence of (I).

Identifying a modulator of phosphatase activity involves a screening **assay**, which involves, providing a **substrate** having a **phosphorylated** residue, preferably **phosphorylated** serine/threonine residue, contacting the **substrate** with a phosphatase in the presence and absence of a candidate modulator of the activity of the phosphatase under conditions which permit **dephosphorylation** of the **substrate** by the phosphatase, contacting the treated substrate with (R), and comparing the binding of (R) to the treated substrate in the presence of (I) with binding of (R) to the treated substrate in the absence of (I).

INDEPENDENT CLAIMS are also included for the following:

(1) a modulator of serine/threonine kinase activity identified by M1;

(2) a screening **assay** for identifying (I) which involves M1;

(3) a kit for identifying (I), comprising serine/threonine kinase, a **substrate** which can be **phosphorylated** by the **kinase**, and (R), or a phosphatase that can dephosphorylate the serine/threonine residue of the **substrate**, a **substrate** having a **phosphorylated** serine/threonine residue and (R);

(4) **assaying** for kinase, preferably serine/threonine kinase

activity, by providing a substrate for kinase, preferably serine/threonine kinase, contacting the substrate with a candidate kinase, preferably serine/threonine kinase, under conditions which permit **phosphorylation** of the **substrate** by a known kinase, contacting the treated substrate with (R), and monitoring the binding of (R) to the treated substrate;

(5) **assaying** for phosphatase activity, by providing a **substrate** having a **phosphorylated** residue, preferably a **phosphorylated** serine/threonine residue, contacting the **substrate** with a candidate phosphatase under conditions which permit **dephosphorylation** of the **substrate** by a known phosphatase, contacting the treated substrate with (R), and monitoring the binding of (R) to the treated substrate;

(6) a kit for **assaying** serine/threonine kinase activity, comprising a **substrate** which can be **phosphorylated** by a serine/threonine kinase and (R); and

(7) a kit for **assaying** phosphatase activity, comprising a **substrate** having a **phosphorylated** serine/threonine residue and (R).

USE - The method is useful for identifying a modulator of serine/threonine kinase activity and phosphatase activity (claimed).

ADVANTAGE - Use of recombinant proteins or synthetic peptides provide an economical, rapidly generated, non-exhaustible supply of reporter, offering considerable practical advantage over antibodies.

Dwg.0/0

TECH UPTX: 20010518

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Binding of (R) to (S) causes or allows a signal to be generated for measuring the binding of (R) to (S). M1 further involves immobilizing the substrate in a flow cell or on magnetic particles e.g., magnetic beads, to allow recording of the signal. The signal generated is a non-radioactive signal, luminescent signal or electrochemiluminescent signal. The magnetic particles are captured magnetically. The substrate is **biotinylated** and is immobilized by interaction with streptavidin, histidine tagged and immobilized by interaction with nickel chelate, or fused to a fusion domain and immobilized by interaction with a antibody which recognizes the fusion domain.

Preferred Protein: (R) is a recombinant protein or a synthetic peptide, and binds directly to a **phosphorylated** residue in the **substrate** or to the **phosphorylated** residue substantially independent of the amino acid sequence either side of the phosphorylated residue. (R) comprises a 14-3-3 protein, amino acid residues of 14-3-3 protein, its fragment or derivative which retains phosphoserine residue binding activity. (R) further comprises a protein having one or both of the amino acid motifs KNVIGAKR and RY, which are highly conserved in 14-3-3 proteins, a WW domain, a fragment or its derivative which retains phosphoserine residue or phosphothreonine residue binding activity. (R) further comprises a stable ruthenium metal chelate which generates electrochemiluminescence in the presence of tripropylamine when a voltage is applied to the stable ruthenium metal chelate.

L24 ANSWER 7 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-159725 [16] WPIDS
DNC C2001-047559
TI Novel double labeled biomolecular substrate, comprising core molecular backbone, covalently labeled with first fluorescent dye and second dye, is useful for **assaying** covalent structural modifications of biomolecules.
DC B04 D16
IN BLUMENTHAL, D K

PA (UTAH) UNIV UTAH RES FOUND
CYC 95
PI WO 2001007638 A2 20010201 (200116)* EN 34p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000076271 A 20010213 (200128)
EP 1206699 A2 20020522 (200241) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2001007638 A2 WO 2000-US40495 20000727; AU 2000076271 A AU 2000-76271 20000727; EP 1206699 A2 EP 2000-965572 20000727, WO 2000-US40495 20000727
FDT AU 2000076271 A Based on WO 200107638; EP 1206699 A2 Based on WO 200107638
PRAI US 1999-145755P 19990727
AB WO 200107638 A UPAB: 20010323
NOVELTY - A biomolecular substrate (I), comprising a core molecular backbone (Ia), a fluorescent dye (Ib) associated with (Ia), and a second dye (Ic) associated with (Ia), is new. When (I) is not covalently modified, (Ic) associates with (Ib) forming a quenched intramolecular dimer, but which, when (I) is covalently modified dissociates from (Ia).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) **assaying** protein kinase activity, comprising:

(a) providing a biomolecular substrate containing a kinase-inducible domain (KID) peptide sequence, a fluoresecein molecule, and a tetramethylrhodamine molecule that associates with the fluorescein to form a intramolecular dye dimer when the **substrate** is **unphosphorylated**, and dissociates when the **substrate** is **phosphorylated** by protein **kinase**;

(b) providing a sample;

(c) introducing the substrate to the sample; and

(d) quantifying a resultant change in fluorescence or absorbance of the biomolecular substrate;

(2) identifying substrates of novel enzymes which catalyze covalent structural modifications of particular proteins or nucleic acids, comprising:

(a) gathering a combinatorial library of unique double-labeled substrates, each comprising:

(i) a randomized core amino acid sequence;

(ii) a fluorescent dye associated with the sequence of (i); and

(iii) a dye associated with the sequence of (i), which associates with the dye of (ii) when the substrates are not covalently modified, forming a quenched intramolecular dye dimer and affecting the fluorescence or absorbance characteristics of the substrate, but dissociates from the dye when the substrates are covalently modified;

(b) systematically contacting each substrate with a novel enzyme;

(c) quantifying any change in fluorescence or absorbance characteristics of each substrate;

(d) selecting members of the library undergoing a change; and

(e) determining the sequence of the selected members; and

(3) a kit comprising a container, one or more (I), and a sample of enzyme standard to standardize the **assay**.

USE - (I) is useful for **assaying** covalent biomolecular modification in a sample (I) is useful for **assaying** protein kinase activity. The method involves providing a sample, introducing the protein kinase substrate to the substrate and quantifying a resultant change in fluorescence or absorbance of (I). The quantification is carried

out separating (I) which has been phosphorylated from (I) which has not been phosphorylated. (I) is also useful for identifying substrates of novel enzyme which catalyze covalent structural modifications of particular proteins or peptide sequences. (All claimed). Monitoring the biomolecular structural modification activities in living cell is used for purposes of basic research, drug discovery, diagnosis of disease states or efficacy of therapy following targeted drug treatment. (I) is also useful for diagnostic and therapeutic applications and for the discovery of activators and inhibitors of novel protein kinases. The **assays** are useful for detecting and quantifying a wide range of covalent biomolecular modifications which do not result in the cleavage of the biomolecule.

ADVANTAGE - **Assaying** covalent biomolecular modifications using (I) has advantages over currently used **assays** in terms of simplicity, throughput, versatility and economy. (I) enables homogeneous and continuous **assay** methods which may be employed both in vitro and in living cells. The **assays** involving (I) are sensitive and homogeneous and do not require the use of radioisotopes. The **assays** are relatively simple and economical adaptable to a wide variety of applications, easily used in vitro and in living cells and allow continuous, real time monitoring of structural modifications to biomolecules.

Dwg.0/9

TECH UPTX: 20010323

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Substrate: (Ia) is a peptide, protein, nucleic acid, sugar, lipid, a receptor or a biopolymer. (Ia) preferably comprises an amino acid sequence and includes a substrate determinant such as a protein kinase substrate. Alternatively, (Ia) includes a nucleotide sequence, a lipid, or a biopolymer comprising a covalent combination of molecules such as amino acids, nucleic acids, sugars or lipids. (I) further comprises spacer segments at either end of (Ia). (I) preferably comprises a KID peptide sequence as (Ia), fluorescein-succinimidyl ester as (Ib) and tetramethylrhodamine-maleimide as (Ic).

Preferred Method: In the method of (1), (I) is introduced into the living cells which include a drug, targeting a specific process of covalent biomolecular modification. Preferably, two or more different (I), each of which is being specific for different process of covalent biomolecular modification and having unique and distinguishable spectral properties, is provided to the sample. Quantifying the resulting change in fluorescence or absorbance characteristics of (I) involves quantifying the resultant change in fluorescence or absorbance of (I) without separating (I) which has been covalently modified from (I) which has not been covalently modified.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Dyes: (Ib) and (Ic) are fluorescent dyes such as fluorescein, rhodamine, cyanine, Oregon Green, Texas Red, Lucifer Yellow, BODIPY, rhodol, coumarin, pyrene, eosin, erythorosine, napthalene, pyridyloxazole, anthrancene, fluorescamine, acridine, benzofuran, anthranilic acid, aminobenzoic acid, N-methylisatoic acid, isoluminol, bezoxadiazole, carboxybenzoyl-quinoline-carboxyaldehyde, salicylate, bimane, phenathroline, Yellow Fluorescent Protein or Green Fluorescent Protein.

L24 ANSWER 8 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-061328 [07] WPIDS
DNC C2001-016947
TI New bisnaphthalene urea compounds, useful e.g. as insulin receptor kinase activators and glucose uptake enhancers for treating hyperglycemia and type I and II diabetes.

DC B05
IN KOZLOWSKI, M R; LUM, R T; MANCHEM, P; SCHOW, S R; SHI, S; SPEWAK, W; SPEVAK, W; MANCHEM, P V V S V; SPEVAK, W R
PA (TELI-N) TELIK INC
CYC 94
PI WO 2000071506 A2 20001130 (200107)* EN 104p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000051684 A 20001212 (200115)
EP 1181271 A2 20020227 (200222) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001005713 A 20011220 (200223)
CZ 2001004153 A3 20020515 (200241)
BR 2000011550 A 20020604 (200246)
KR 2002022679 A 20020327 (200264)
US 6458998 B1 20021001 (200268)
HU 2002001306 A2 20020930 (200272)
CN 1364156 A 20020814 (200280)
ADT WO 2000071506 A2 WO 2000-US14644 20000525; AU 2000051684 A AU 2000-51684 20000525; EP 1181271 A2 EP 2000-936360 20000525; WO 2000-US14644 20000525; NO 2001005713 A WO 2000-US14644 20000525, NO 2001-5713 20011123; CZ 2001004153 A3 WO 2000-US14644 20000525, CZ 2001-4153 20000525; BR 2000011550 A BR 2000-11550 20000525, WO 2000-US14644 20000525; KR 2002022679 A KR 2001-715133 20011126; US 6458998 B1 Provisional US 1999-136128P 19990526, US 2000-579279 20000525; HU 2002001306 A2 WO 2000-US14644 20000525, HU 2002-1306 20000525; CN 1364156 A CN 2000-810853 20000525
FDT AU 2000051684 A Based on WO 200071506; EP 1181271 A2 Based on WO 200071506; CZ 2001004153 A3 Based on WO 200071506; BR 2000011550 A Based on WO 200071506; HU 2002001306 A2 Based on WO 200071506
PRAI US 1999-136128P 19990526; US 2000-579279 20000525
AB WO 200071506 A UPAB: 20021105
NOVELTY - Bisnaphthalene urea compounds (I) and their salts, single stereoisomers and mixture of stereoisomers are new.

DETAILED DESCRIPTION - Bisnaphthalene urea compounds of formula (I) and their salts, single stereoisomers and mixture of stereoisomers are new.

R1, R2 are substituents on the A ring and are SO2N(R7)2, C(O)N(R7)2, NR7SO2R7, NR7C(O)R7, SO2OR7, C(O)OR7, OSO2R7 or OC(O)R7;

R3, R4 = H or lower alkyl; or

R3+R4 = (CH2)n; or

R3 or R4 = an electron pair,

n = 2-4;

R5, R6 = H, optionally substituted alkyl, cyano, halo, nitro, SR8, C(O)R8, SO2OR8, OSO2R8, SO2N(R8)2, NR8SO2R8, OC(O)R8, C(O)OR8, C(O)NR8, NRC(O)R8, OR8 or N(R8)2;

R7, R8 = H; alkyl, aryl, aryl(lower)alkyl, heteroaryl(lower)alkyl, heterocyclyl or heteroaryl (all optionally substituted);

Y = a non-interfering substituent which is not linked to the naphthalene ring via an azo or amide linkage;

x = 0-2;

the linker connects a carbon designated as c to a carbon designated as d and is N(R3)(C=K)N(R4), N=C(N(R asterisk)2)N(R4), N(R3)C(N(R asterisk))2=N, N=C(SR')N(R4), N(R3)C(=SR'')N(R4) or N(R3)C(SR')=N;

R' = H, CN or lower alkyl;

R'' = CN or lower alkyl;
K = O, S or NR asterisk ;
R asterisk H or lower alkyl;
provided that if R1 = R2 = SO2OH, then:
(i) no Y is SO2OH;
(ii) neither R5 nor R6 is SO2OR8 or OSO2R8; and
(iii) R5 and R6 are not both selected from OH and H unless at least one (Y)x is (Y')x';
x' = 1 or 2; and
Y' = halo.

INDEPENDENT CLAIMS are included for the following:

(A) stimulating or activating the kinase activity of the insulin receptor comprising contacting the insulin receptor or the kinase portion of the insulin receptor with (I);

(B) stimulating the uptake of glucose into cells displaying the insulin receptor, comprising contacting the cells with (I);

(C) use of (I) in the preparation of a medicament for treating or preventing mammalian disease state selected from hyperglycemia, type I diabetes and type II diabetes;

(D) preparation of (I)

(E) use of (I) for treating type I and late stage type II diabetes, comprising co-administering with a potentially sub-therapeutic dose of insulin in order to achieve therapeutic efficacy;

(F) preparation of compounds which mimic the function of (I);

(G) radiolabeled (I).

ACTIVITY - Antidiabetic; hypoglycemic.

3-(((7-((N-(7-(((3-Sulfophenyl)amino)sulfonyl)-2-naphthyl)-carbamoyl)amino)-2-naphthyl)sulfonyl)amino)benzenesulfonic acid (Ia) caused 20% reduction of blood glucose over 1 hour when administered orally at 30 mg/kg to STZ/HFD rat model of type II diabetes.

MECHANISM OF ACTION - Insulin receptor kinase activator; insulin receptor activator; glucose uptake enhancer.

((I) activate the insulin receptor by stimulating autophosphorylation of the receptor, mainly at a specific portion of the receptor, the beta -kinase domain).

In a 32P-cytoplasmic kinase domain (CKD) autophosphorylation assay, in which the potency of a compound to increase phosphorylation was expressed as % of the vehicle level, (Ia) exhibited 135% activity. In a glucose transport activity assay using 3T3 L1 fibroblasts (ATCC), stimulation of the insulin receptor leading to the transport of glucose from the blood into cells to modify blood glucose levels was measured. The concentration of compound necessary to produce an increase in glucose transport to greater than 150% of the vehicle control was determined. The concentration of (Ia) required to reach more than 150% activity of DMSO was 3.2 micro M.

USE - As glucose uptake enhancer for treating hyperglycemia, type I and type II diabetes in mammals. As a model for obtaining and/or developing compounds that have the function of (i) stimulating the kinase activity of the insulin receptor, (ii) activating the insulin receptor and (iii) stimulating the uptake of glucose; for validating, optimizing or standardizing bioassays. Radiolabeled (I) are used as diagnostics for identifying and/or obtaining compounds that have the function of (i)-(iii) (all claimed). Radiolabeled (I) may used to diagnose diabetes in patients displaying pre-diabetic risk factors e.g. Syndrome-X.

ADVANTAGE - Co-administration of (I) with sub-therapeutic doses of insulin minimizes the possibility of the diabetic patient over-dosing on insulin and suffering from the severe consequences e.g. coma and death. (I) are incapable of inducing hypoglycemia in the presence or absence of insulin. (I) increase the effectiveness of insulin, but do not display true insulin mimetic effects (e.g. hypoglycemia) making them effective

insulin safeners.
Dwg.0/14

TECH UPTX: 20010202
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Claimed preparation of (I) comprises:
(1) intermolecular or intramolecular condensation of a compound of formula (II) with a compound of formula (III) or the addition of (II) to (III), where the amino groups of (II) and (III) are optionally in a protected form, with an activated bifunctional reaction that provides the group K=C, to form a linker between (II) and (III).
WZ = S=C= or O=C=; or
W, Z = as for R3 or R4.
Compounds (I) are interconvertible.
In (F), preparation of compounds which mimic the function of (I) comprises:
(aa) submitting a test compound to a screen for determining its stimulation of the kinase activity of the insulin receptor in relation to (I); and
(bb) preparing the test compound if it exhibits stimulation of the kinase activity of the insulin receptor.

L24 ANSWER 9 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-579365 [54] WPIDS
DNN N2000-428700 DNC C2000-172510
TI New isolated polypeptide having the sequence of dual-specificity phosphatase-1 (DSP-1) is useful for treating a patient with a disorder associated with DSP-1 activity e.g. cancer and autoimmune diseases.
DC B04 D16 S03
IN LUCHE, R M; WEI, B
PA (CEPT-N) CEPTYR INC
CYC 90
PI WO 2000053636 A2 20000914 (200054)* EN 74p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000036217 A 20000928 (200067)
ADT WO 2000053636 A2 WO 2000-US6154 20000308; AU 2000036217 A AU 2000-36217 20000308
FDT AU 2000036217 A Based on WO 200053636
PRAI US 1999-123255P 19990308
AB WO 200053636 A UPAB: 20001027
NOVELTY - An isolated polypeptide (I) having the 198 amino acid sequence of dual-specificity phosphatase-1 (DSP-1) given in the specification, or a variant that differs in one or more amino acid deletions, additions, insertions or substitutions at no more than 50 % of the residues in the given sequence, is new. The polypeptide has the ability to dephosphorylate an activated mitogen-activated protein (MAP)-kinase.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polynucleotide (II) that encodes at least 10 consecutive amino acids of a polypeptide sequence corresponding to the 198 amino acid sequence given in the specification;
(2) an expression vector (III) comprising (II);
(3) a host cell (IV) transformed or transfected with (III);
(4) an antisense polynucleotide (V)comprising at least 15 consecutive nucleotides complementary to (II);
(5) producing a DSP-1 polypeptide comprising:

(a) culturing (IV); and
(b) isolating DSP-1 polypeptide from the culture;
(6) an isolated antibody or antigen binding fragment (VI) that specifically binds to a DSP-1 polypeptide;
(7) a method (M1) for detecting DSP-1 expression in a sample comprising:
(a) contacting a sample with (VI) ; and
(b) detecting the level of antibody/DSP-1 complex;
(8) a method (M2) for detecting DSP-1 expression in a sample comprising:
(a) contacting a sample with (V); and
(b) detecting the amount of DSP-1 polynucleotide that hybridizes to (V);
(9) a method (M3) for screening for an antigen that modulates DSP-1 activity comprising:
(a) contacting a candidate agent with (I); and
(b) evaluating the ability of the polypeptide to **dephosphorylate** a DSP-1 **substrate** relative to a predetermined ability of the polypeptide to **dephosphorylate** the DSP-1 **substrate** in the absence of candidate agent;
(10) a method (M4) for screening for an agent that modulates DSP-1 activity comprising:
(a) contacting a candidate agent with a cell comprising a DSP-1 promoter operably linked to a polynucleotide encoding a detectable transcript or protein;
(b) evaluating expression of the polynucleotide, relative to a predetermined level of expression in the absence of candidate agent;
(11) a DSP-1 substrate trapping mutant polypeptide;
(12) a method (M5) for screening a molecule for the ability to interact with DSP-1 comprising:
(a) contacting a candidate molecule with (I); and
(b) detecting the presence or absence of binding of the candidate molecule to the polypeptide; and
(13) a method (M6) for modulating a proliferative response in a cell, differentiation of a cell and/or survival of a cell comprising contacting the cell with an agent that modulates DSP-1 activity.
ACTIVITY - Cytostatic; immunosuppressive; antiallergic.
No supporting biological data is given.
MECHANISM OF ACTION - Phosphotyrosine and phosphothreonine/serine dephosphorylator.
No supporting biological data given.
USE - For treating a patient with a disorder associated with DSP-1 activity, especially cancer, graft-versus-host disease, autoimmune diseases, allergies, metabolic diseases, abnormal cell growth, abnormal cell proliferation and cell cycle abnormalities (claimed).
ADVANTAGE - Provides a greater understanding of MAP-kinase signaling and the regulation of DSP within MAP-kinase signaling cascades.
Dwg.0/6

TECH UPTX: 20001027
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polynucleotide: (II) preferably encodes at least 15 consecutive amino acids of the given sequence. The polynucleotide preferably has the 1137 base pair (bp) sequence provided in the specification.
Preferred Antisense Polynucleotide: The antisense polynucleotide preferably hybridizes under conditions which include a wash in 0.1X SSC and 0.1% SDS at 50 degrees Celsius for 15 minutes.
Preferred Antibody: The antibody is preferably a monoclonal antibody.
Preferred Mutant Polypeptide: The mutant polypeptide preferably contains a substitution at position 80 or position 111 of the 198 amino acid sequence given in the specification.

Preferred Method: In M1 the antibody is linked to a support material and a detectable marker. The sample is a biological sample obtained from a patient.
In M2 the amount of DSP-1 polynucleotide which hybridizes to the antisense polynucleotide in determined using polymerase chain reaction (PCR) or a hybridization **assay**. The sample can comprise an RNA or a cDNA preparation.
In M3 the DSP-1 substrate is a MAP-kinase. The candidate agent is a small molecule, preferably present within a combinatorial library.
In M4 the polynucleotide encodes a DSP-1 polypeptide and/or a reporter protein.
In M5 the step of detecting comprises an affinity purification step. The step of detecting comprises a yeast two hybrid screen of a phage display library.
In M6 the agent modulates a pattern of gene expression. The cell displays contact inhibition of cell growth and/or anchorage independent growth. The cell also displays an altered intercellular adhesion property. The agent preferably modulates apoptosis and/or the cell cycle. The cell is preferably present within a patient.

L24 ANSWER 10 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-578538 [54] WPIDS
CR 1997-480219 [44]
DNC C2000-172207
TI Novel ubiquitin dependent kinase which phosphorylates a member of IkappaB family of inhibitor proteins at serine residues 32 and 36, useful for identifying antagonists such that NF-kappaB activation is inhibited.
DC B04 D16
IN CHEN, Z J
PA (LEUK-N) LEUKOSITE INC
CYC 1
PI US 6107073 A 20000822 (200054)* 69p
ADT US 6107073 A CIP of US 1996-616499 19960319, US 1997-825559 19970319
PRAI US 1997-825559 19970319; US 1996-616499 19960319
AB US 6107073 A UPAB: 20001027
NOVELTY - A purified ubiquitin dependent kinase (I) which phosphorylates IkappaB alpha (II) at serine residues 32 and 36, when activated and is a multi subunit complex of approximately 700 kilo Daltons (kDa) as determined by size exclusion chromatography, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a **bioassay** for assessing candidate drugs or ligand of (I) which involves contacting a candidate drug or ligand with a sample containing a kinase, and evaluating the biological activity (the amount of **phosphorylated substrate**, a **labeled** (II), that is produced) modified by the contact. A reduction in the amount of biological activity in the candidate drug or ligand indicates that the candidate drug or ligand is an inhibitor of kinase activity.
ACTIVITY - Antiinflammatory; anti-HIV; cytostatic; antipsoriatic; vasotropic.
No supporting data is given.
MECHANISM OF ACTION - Gene therapy; NFkappaB activation inhibitor.
No supporting biological data is given.
USE - (I) is useful for identifying antagonists against it such that activation of NFkappaB is inhibited and the inhibitors are thus useful for treating inflammation, HIV infection, cancer, sepsis, psoriasis, restenosis and reperfusion injury. The nucleic acid encoding (I) are also useful in treating the above mentioned disorders by gene therapy techniques.
Dwg.6B/24
TECH UPTX: 20001027

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Kinase: (I) when ubiquitinated or **phosphorylates** (II). The **kinase** is purified from cell (HeLa cell) cytoplasmic extracts by chormatographic purification such as ion exchange chromatography and size exclusion chromatography.

L24 ANSWER 11 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-317518 [27] WPIDS
DNC C2000-096036
TI Composition used to facilitate uptake of aminoglycoside antibiotic into cells comprises **phosphoinositide** polyphosphate and/or inositol polyphosphate and polyamine.
DC A96 B05 C03
IN DEWALD, D B; OZAKI, S; PRESTWICH, G D; SHOPE, J
PA (UTAH) UNIV UTAH RES FOUND; (UTAH) UNIV UTAH STATE
CYC 86
PI WO 2000018949 A2 20000406 (200027)* EN 37p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9965026 A 20000417 (200035)
EP 1119315 A2 20010801 (200144) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000018949 A2 WO 1999-US22594 19990929; AU 9965026 A AU 1999-65026 19990929; EP 1119315 A2 EP 1999-952984 19990929, WO 1999-US22594 19990929
FDT AU 9965026 A Based on WO 200018949; EP 1119315 A2 Based on WO 200018949
PRAI US 1999-396296 19990915; US 1998-102482P 19980930
AB WO 200018949 A UPAB: 20000606
NOVELTY - Composition comprises a mixture of a **phosphoinositide** polyphosphate and/or inositol polyphosphate and a polyamine.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) visualizing the uptake and localization of aminoglycoside antibiotics in a cell which comprises mixing an aminoglycoside having a visually identifiable label with a polyamine, contacting the cell with the obtained mixture and observing the label to visualize uptake and localize the aminoglycoside in the cell;

(2) screening for a compound that minimizes the cytotoxicity of aminoglycoside antibiotics to mammalian cells which comprises contacting a cell with a mixture of an aminoglycoside having a label and a polyamine and observing the label, where reduced uptake of the aminoglycoside or altered localization of the aminoglycoside compared to the cell treated with the mixture in the absence of the compound indicates reduced toxicity;

(3) a composition comprising an aminoglycoside antibiotic covalently to a fluorescent compound and

(4) monitoring calcium flux in a cell which comprises loading the cell with a calcium indicator, exchanging the medium and monitoring the cell until no intensity change in the indicator is observed, contacting the cell with a complex Ins(1,4,5)P3 and a shuttle so that the Ins(1,4,5)P3 enters the cell and modulates the calcium indicator and detecting the calcium indicator, where a change of the indicator indicates a change in calcium flux in the cell.

(1) (2) (3) compositions of matter comprising an aminoglycoside antibiotic covalently bonded to a fluorescent compound; and (4) methods for .

USE - The composition is used to facilitate uptake of **phosphoinositide** polyphosphates and/or inositol polyphosphates or aminoglycoside antibiotics (neomycin, gentamicin, geneticin, streptomycin, kanamycin, tobramycin, spectinomycin, formicidin, streptamine, deoxystreptamine, epistreptamine, fortamine, validamine, valienamine, hydroxyvalidamine, valiciamine and/or validoxylamine A, B and/or G) into cells, preferably eukaryotic cells including animal, plant, protozoal, helminthic or fungal cells and prokaryotic cells including those of the genera Escherichia, Pseudomonas, Acinetobacter, Francisella, Bordetella, Shigella, Salmonella, Proteus, Yersinia, Klebsiella, Enterobacter, Serratia, Vibrio, Haemophilus, Pasteurella, Streptobacillus, Bacteroides, Fusobacterium, Neisseria, Staphylococcus, Streptococcus, Corynebacterium, Bacillus, Clostridium, Nocardia, Actinomyces, Mycobacterium, Rickettsia, Chlamydia, Spirillum, Campylobacter, Treponema, Borrelia, Leptospira, Helicobacter and Mycoplasma.

The composition is used to visualize the location of fluorescently **labeled phosphoinositides** during changes in cell physiology, to screen inhibitors of changes in cell physiology, to visualize the uptake and localization of aminoglycosides, to develop selectivity **assays** by observing the selective uptake of fluorescent aminoglycosides in pathogens versus human or animal cells, to identify new therapeutic compounds that can affect the selectivity of aminoglycoside uptake, to provide a high-throughput screen for natural and synthetic products that affect cellular uptake and targeting of both aminoglycosides and **phosphoinositides** to cells from vertebrate tissues versus cells of pathogenic organisms, to use PIPn-fluorescent aminoglycoside uptake for the visualization of uptake and sub-cellular localization of aminoglycosides and to develop antibiotic selectivity **assays** by observing selective uptake of fluorescent aminoglycosides in pathogens including bacteria, protozoal parasites against human or animal cells.

The composition can be used to implement high-throughput screening for identifying agonists and antagonists for protein **kinases** and **phosphoinositide kinases** and for **phosphoinositide** and inositol phosphate binding proteins that are regulated by PIPns or IPns and may serve as downstream effectors in signaling pathways important for therapeutic interventions including cell-based **assays** using intracellular PIPns introduced by the shuttling system and using primary cells, immortalized cells, cancer cells, cells transformed with plasmids encoding key enzymes or other proteins as well as in vitro cell extracts or partially purified or homogeneous proteins.

Dwg.0/0

TECH UPTX: 20000606

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred composition: The polyamine comprises an aminoglycoside, dendrimeric polyamine, histone, polybasic polypeptide, lipidic polyamine, polyethyleneimine and/or steroidal polyamine. At least one of the **phosphoinositide** polyphosphate and/or inositol polyphosphate is labeled with a detectable label, preferably a fluorescent, radio, chemiluminescent or spin label, a photophore, chromophore, nanogold particle and/or **biotin**. The fluorescent label comprises acrylodan, AMCA, BODIPY, Cascade-Blue, CINERF, dansyl, dialkylaminocoumarin, eosin, erythrosine, fluorescein, hydroxycoumarin, NBD, Oregon green, PyMPO, pyrene, rhodamine, Rhodol Green, TMR, Texas Red or X-Rhodamine.

L24 ANSWER 12 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-195583 [17] WPIDS
CR 2000-195582 [17]; 2000-205722 [18]
DNN N2000-144644 DNC C2000-060780

TI Novel kappa B-kinase related kinases IKR-1 and IKR-2 used as molecular weight markers and in peptide fragmentation studies.

DC B04 D16 S03

IN BIRD, T A; VIRCA, G D

PA (IMMV) IMMUNEX CORP

CYC 88

PI WO 2000008179 A1 20000217 (200017)* EN 85p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9952527 A 20000228 (200030)
EP 1019513 A1 20000719 (200036) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002524047 W 20020806 (200266) 76p

ADT WO 2000008179 A1 WO 1999-US17578 19990804; AU 9952527 A AU 1999-52527 19990804; EP 1019513 A1 EP 1999-937763 19990804, WO 1999-US17578 19990804; JP 2002524047 W WO 1999-US17578 19990804, JP 2000-563802 19990804

FDT AU 9952527 A Based on WO 200008179; EP 1019513 A1 Based on WO 200008179; JP 2002524047 W Based on WO 200008179

PRAI US 1999-118783P 19990205; US 1998-95269P 19980804; US 1998-99973P 19980911

AB WO 200008179 A UPAB: 20021014

NOVELTY - Nucleic acids encoding novel kappa B-kinase related kinases, designated IKR-1 and IKR-2, are new.

DETAILED DESCRIPTION - A novel isolated IKR-1 or IKR- 2 nucleic acid (NA) (I), selected from:

(a) the defined 3385 base pair (bp) or 3219 bp sequences given in the specification;

(b) a NA encoding the defined 717 or 729 amino acid sequences given in the specification;

(c) a NA that hybridizes to either strand of a denatured, DNA molecule comprising the sequence of (a) or (b) under moderately stringent conditions (e.g. 50% formamide, 6XSSC (saline sodium citrate) at 42 deg. C, and washing in 0.5XSSC and 0.1% SDS (sodium dodecyl sulfate) at 60 deg. C);

(d) a NA derived by in vitro mutagenesis of (a);

(e) a NA degenerate from (a) as a result of the genetic code; and

(f) a NA selected from mouse IKR-1 or IKR-2 DNA, human IKR DNA, allelic variants of mouse or human IKR DNA, and a species homologs of IKR DNA.

INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant vector that directs the expression of (I);

(2) an isolated polypeptide (II) encoded by (I), preferably having a molecular weight of 81 or 83 kDa as determined by SDS-PAGE (SDS-polyacrylamide gel electrophoresis) and in a non-glycosylated form, which is especially a protein kinase;

(3) isolated (monoclonal) antibodies to (II);

(4) host cell transfected or transduced with the vector of (1);

(5) a method for the production of a IKR-1 or IKR-2 polypeptide, comprising culturing the cell of (4) in suitable culture medium under conditions promoting gene expression, and recovering the polypeptide from the culture medium (preferably the host cell is selected from bacteria, yeast, plant or animal cells);

(6) a method for determining the molecular weight (MW) of a sample protein, comprising comparison of the MW of the sample proteins with the MW of (II), wherein the comparison comprises:

(i) application of the sample protein and (II) to an acrylamide gel;

(ii) resolution of the sample protein and (II) using an electric current; and

(iii) application of a reagent for detecting the sample protein and (II);

(7) a kit for detecting the MWs of peptide fragments of a sample protein, comprising:

(i) a vessel;

(ii) polypeptide (II);

(iii) at least one enzyme selected from Asparaginylendopeptidase, Arginylendopeptidase, Achrombobacter protease I, Trypsin, Staphylococcus aureus V8 protease, Endoproteinase Asp-N, and Endoproteinase Lys-C;

(iv) a mutant of (II) derived by in vitro mutagenesis, wherein a site of enzyme cleavage on (II) has been removed; and

(v) fragmented peptides derived from (II) by enzymatic cleavage with the selected enzyme, wherein the sample protein and (II) are contacted with the same enzyme, and the fragments are detected by the method of (6);

(8) a DAKAR (undefined) polypeptide comprising amino acids 1-300 of a defined 717 or 729 amino acid sequence given in the specification;

(9) a method of determining protein kinase activity in which the protein kinase moiety is (II) or the polypeptide of (8);

(10) a method for identifying substances that affect phosphorylation, comprising:

(i) providing a substance suspected of affecting phosphorylation activity;

(ii) adding (in any order) a peptide or protein **substrate** to be **phosphorylated**, a polypeptide **kinase** consisting of IKR-1 (comprising the 717 amino acid sequence given in the specification), IKR-2 (comprising the 729 amino acid sequence given in the specification), an active domain or fragment thereof, and a source of phosphates;

(iii) incubating for a time and conditions sufficient for kinase-mediated transfer of a phosphate to the substrate;

(iv) measuring the amount of phosphate transferred; and

(v) comparing the amount of phosphate transferred to that transferred in the presence of a standard substance of known phosphorylation-affecting ability;

(11) a method for identifying substances that interfere with the activation of NF-kappaB, comprising:

(i) providing a substance suspected of interfering with the activation of NF-kappaB;

(ii) adding (in any order) peptide or protein substrates to be phosphorylated, a polypeptide kinase consisting of IKR-1 (comprising the 717 amino acid sequence given in the specification), IKR-2 (comprising the 729 amino acid sequence given in the specification), an active domain or fragment thereof, adenosine triphosphate (ATP), a gene with an intact promoter that is activated by NF-kappaB and all other factors necessary for transcription;

(iii) incubating for a time and conditions sufficient for kinase function and transcription of the gene;

(iv) measuring the amount of transcript made;

(v) comparing the amount of transcript made to that made to a standard to determine is the substance interferes with NF- kappaB activation;

(12) a method of designing a molecule that inhibits or enhances the kinase activity of (II), comprising:

(i) determining the three dimensional structure of the polypeptide;

(ii) analyzing this structure for likely binding sites of substrates;

(iii) synthesizing a molecule that incorporates a predictive reactive site; and

(iv) determining the kinase-inhibiting activity or kinase- enhancing activity of the molecule, respectively.

ACTIVITY - Immunomodulatory; antiinflammatory; antimicrobial; cytostatic.

No biological data given.

MECHANISM OF ACTION - The protein function as kinases.

USE - The kappa B-kinase related kinase IKR-1 and IKR- 2 polynucleotides can be used to express the polypeptides, and as probes to identify nucleic acids encoding proteins having kinase activity. IKR-1 and IKR-2 polypeptides and fragmented polypeptides are used for purifying proteins, e.g. to purify binding partner proteins; to measure protein activity, e.g. as quality assurance agents to monitor shelf life and stability of binding partner proteins. They may also be used as research agents, e.g. in assays to determine protein kinase activity, to identify novel molecules involved in signal transduction pathways, and to identify therapeutic compounds, to identify substances which interfere with the rate of substrate phosphorylation (such compounds would be useful for the treatment of autoimmune, inflammatory, infectious or neoplastic diseases), as molecular weight and isoelectric focusing markers, as controls for peptide fragmentation, identification of unknown proteins, e.g. by comparison with proteins in databases and for preparation of antibodies. The antibodies can be used in assays to detect the presence of the protein, and to purify the protein by immunoaffinity chromatography. The antibodies can also be used to block binding of the IKR polypeptides to their binding partners.

ADVANTAGE - A need exists for polypeptides suitable for use in peptide fragmentation studies, for use in molecular weight measurements, and for use in protein sequencing using tandem mass spectroscopy. This need is met by the present invention.

Dwg.0/4

TECH UPTX: 20000405

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The nucleic acids and the proteins they encode may be prepared according to standard methodologies.

L24 ANSWER 13 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-160373 [14] WPIDS
DNC C2000-049996
TI Fungal inositolphosphorylceramide synthase inhibitor **assay** for identifying compounds useful in antifungal chemotherapy, comprises measuring inhibition of ceramide conversion to **phosphoinositol** ceramide by test compound.
DC B04 D16 K08
IN DICKSON, R C; LESTER, R L; RADDING, J
PA (ELIL) LILLY & CO ELI; (KENT) UNIV KENTUCKY RES FOUND
CYC 1
PI US 6022684 A 20000208 (200014)* 12p
ADT US 6022684 A Provisional US 1996-28079P 19961007, US 1997-944594 19971006
PRAI US 1996-28079P 19961007; US 1997-944594 19971006
AB US 6022684 A UPAB: 20000320

NOVELTY - A fungal inositolphosphorylceramide (IPC) synthase inhibitor **assay**, is new.

DETAILED DESCRIPTION - A fungal inositolphosphorylceramide (IPC) synthase inhibitor **assay** comprises:

(a) recombinantly expressing Saccharomyces IPC1 gene in cells transformed to express the gene, where the cells are in a homogenous culture and located in a container;

(b) introducing excess ceramide and **phosphatidylinositol**, where the ceramide or **phosphatidylinositol** carry a **label** for identification, and a test compound to the container;

(c) subjecting the container and contents to ordinary conditions

necessary for ceramide conversion to **phosphoinositol** ceramide; and

(d) identifying those test compounds which inhibit ceramide conversion to **phosphoinositol** ceramide.

An INDEPENDENT CLAIM is also included for a method which determines the ability of a test compound to inhibit IPC synthase comprising:

(a) introducing excess **biotinylated** ceramide, **labeled phosphatidylinositol** and test compound into a container containing untransformed cells that express IPC synthase;

(b) subjecting the contents of the container to ordinary conditions necessary for ceramide conversion to **phosphoinositol** ceramide; and

(c) identifying those test compounds which inhibit ceramide conversion to **phosphoinositol** ceramide.

USE - The **assay** is useful for identifying inhibitors of IPC synthase which are likely candidates for antifungal chemotherapy.

Dwg.0/3

TECH UPTX: 20000320

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The IPC1 gene is over-expressed. The cells are chosen from Escherichia coli, Saccharomyces cerevisiae, and S. pombe. The labeled starting substrate is a 2-12C ceramide such as 4-nitobenzo-2oxa-1,3-diazole (NBD)-6C-ceramide, 8-methyl-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-3-indacene (BODIPY)-5C-ceramide or N-hexanoyl-sphingosine. The 2-12C ceramide is labeled with a fluorescent or radioactive (3H or 14C) material.

The method comprises introducing excess **biotinylated** ceramide, **labeled phosphatidylinositol** and a test compound to the container in step (b). After ceramide conversion to **phosphoinositol** ceramide, the **biotinylated** ceramide is conjugated to streptavidin derivatized solid substrate followed by step (d).

Alternatively, the method comprises introducing excess **biotinylated** ceramide, **phosphatidylinositol** and a test compound to the container in step (b). After ceramide conversion to **phosphoinositol** ceramide, the **biotinylated** ceramide is conjugated to labeled streptavidin derivatized solid substrate capable of filter separation, followed by filtering to isolate the labeled streptavidin derivatized solid substrate. Those test compounds which inhibit ceramide conversion to **phosphoinositol** ceramide are then identified.

The solid substrate are **scintillation** proximity **assay** (SPA) beads. The **phosphatidylinositol** is **labeled** with tritium or **32P**.

L24 ANSWER 14 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-147265 [13] WPIDS
DNC C2000-046101
TI Novel polyphosphates useful as reagents for kinase **assays**.
DC A96 B04 D16 K08
IN PRESTWICH, G D
PA (UTAH) UNIV UTAH RES FOUND
CYC 86
PI WO 2000000584 A2 20000106 (200013)* EN 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9947240 A 20000117 (200026)

ADT WO 2000000584 A2 WO 1999-US14566 19990626; AU 9947240 A AU 1999-47240 19990626
FDT AU 9947240 A Based on WO 200000584
PRAI US 1998-90922P 19980626
AB WO 200000584 A UPAB: 20000313
NOVELTY - **Scintillant**-tethered **phosphoinositide** polyphosphates are useful as reagents for kinase **assays**.
DETAILED DESCRIPTION - Compositions comprising (I) or (II) are new: PIPn-L-S (I); PIPn-L-S-Matrix (II);
PIPn = a **phosphoinositide** polyphosphate;
L = a linker moiety;
S = a **scintillant**; and
Matrix = a solid support.
INDEPENDENT CLAIMS are also included for following:
(1) a method for **assaying** a **phosphatidylinositol kinase**, comprising contacting (II) with effective amounts of a sample to be tested, containing (II), reaction buffer, and ATP labeled with a low-energy beta emitter, to form a reaction mixture, incubating the mixtures, so that the PIPn is phosphorylated, and the low-energy beta emitter is coupled, radioactive decay of which induces emission of light by the **scintillant**, and detecting the light; and
(2) a method for screening compounds for a drug which interferes with **phosphatidylinositol kinase** activity, comprising the method above, where the detected light is compared to a control, decreases in light in the presence of the compound indicates interference with the kinase activity.
USE - (II) are useful for **assaying** PIKs and for screening compounds for inhibition of PIK activity (claimed).
Dwg.0/12
TECH UPTX: 20000313
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: PIPn is **phosphatidylinositol**, **phosphatidylinositol** 3-, 4- or 5-phosphate, or phosphatidylinositiol 4,5-bisphosphate or 3,4,5-triphosphate. L is a hydrophilic linker moiety, preferably a succinimide or poly(ethylene glycol), e.g. hexa(ethylene glycol) or PEG 3,400. S is 2-(4-amino-methylphenyl)-5-(4-biphenyl)-1,3,4-oxadiazole. The matrix comprises a hydrophobic polymer, e.g. polystyrene, preferably in the form of a microtitre plate.
Preferred Preparation: (I) is prepared by activating the **scintillant**; reacting it with the linker moiety; then activating the intermediate formed and reacting it with an aminoacyl-PIPn to give (I).

L24 ANSWER 15 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-633831 [54] WPIDS
DNC C1999-185115
TI New polypeptides that **phosphorylate kinase**, used to screen for modulators for treating e.g. cancer or inflammation.
DC B04 D16
IN BERMAN, K; CHEN, Z; COBB, M; HUTCHINSON, M; HUTCHISON, M
PA (TEXA) UNIV TEXAS SYSTEM
CYC 86
PI WO 9953076 A1 19991021 (199954)* EN 94p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9935605 A 19991101 (200013)

BR 9909679 A 20001219 (200103)
US 6165461 A 20001226 (200103)
EP 1071787 A1 20010131 (200108) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1303435 A 20010711 (200159)
JP 2002515223 W 20020528 (200238) 124p

ADT WO 9953076 A1 WO 1999-US8165 19990414; AU 9935605 A AU 1999-35605 19990414; BR 9909679 A BR 1999-9679 19990414, WO 1999-US8165 19990414; US 6165461 A US 1998-60410 19980414; EP 1071787 A1 EP 1999-917495 19990414, WO 1999-US8165 19990414; CN 1303435 A CN 1999-806761 19990414; JP 2002515223 W WO 1999-US8165 19990414, JP 2000-543623 19990414

FDT AU 9935605 A Based on WO 9953076; BR 9909679 A Based on WO 9953076; EP 1071787 A1 Based on WO 9953076; JP 2002515223 W Based on WO 9953076

PRAI US 1998-60410 19980414

AB WO 9953076 A UPAB: 19991221

NOVELTY - Polypeptides (I) capable of phosphorylating MEK3 (a MAP/ERK kinase) are new.

DETAILED DESCRIPTION - (I) have sequences (S1) or (S2) of 1001 or 993 amino acids (aa), respectively or are variants of these with practically the same ability to phosphorylate MEK3 (sequences are given in the specification).

INDEPENDENT CLAIMS are also included for the following:

(a) a conditionally active variant (Ia) of (I);

(b) a polypeptide that can phosphorylate MEK3 but not MEK1 or 2;

(c) isolated nucleic acid (II) encoding (I) or (Ia);

(d) any of 12 sequences (IIb) (given in the specification), or their variants, encoding polypeptides (Ib) able to phosphorylate MEK3;

(e) (Ib);

(f) recombinant expression vector containing (II) or (IIb);

(g) host cells transformed or transfected with these vectors;

(h) nucleic acid (IIa) of at least 10 nucleotides (nt) complementary to (II) or (IIb);

(i) a composition containing (I), (II), (IIa) or (IIb) plus a carrier;

(j) method for phosphorylating MEK3, 4 or 6, or their variants, using (I) or (Ib);

(k) method for activating a stress-responsive MAP kinase pathway by administering (I) or (Ib);

(l) method for identifying agents (A) that modulate signal transduction via a stress-responsive MAP kinase pathway;

(m) monoclonal antibodies (MAb), or their antigen-binding fragments that bind specifically to (I) or (Ib);

(n) a composition containing MAb or its fragments;

(o) treating diseases associated with stress-responsive MAP kinase pathways by administering (A);

(p) detecting presence of a TAO kinase from its ability to phosphorylate MEK3 polypeptide; and

(q) kits for this process.

ACTIVITY - Anti-inflammatory; anticancer; antidiabetic; antidegeneration.

MECHANISM OF ACTION - (I) regulates MAP kinase pathways that are involved in cell proliferation, oncogenesis, development and cell differentiation.

USE - (I), designated TAO kinases, and related polypeptides, are used to screen for modulators of stress-responsive MAP kinase pathways. These modulators are potentially useful for treating or preventing:

(1) inflammation, autoimmune disease, cancer and degeneration (inhibitors of phosphorylation), or

(2) insulin-resistant diabetes, metabolic disorders and neurodegeneration (enhancers of phosphorylation).

(I) are also used to raise specific antibodies, useful therapeutically as modulators and as **immunoassay** reagents for detecting (I). Nucleic acid (II) that encodes (I) can be used:

(a) for recombinant expression of (I), and

(b) in the form of fragments, for detecting (II) in standard hybridization and amplification tests.

ADVANTAGE - (I) are highly specific for MEK3.

Dwg.0/0

TECH UPTX: 19991221

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Proteins: (I) is (S1) or (S2), designated TAO 1 and 2, respectively, or differs from these only in conservative substitutions and/or modifications. A particularly preferred (I) contains aa 1-416 of (S1).

Preferred Nucleic Acid: These are sequences of 3312 bp (S3) and 4296 bp (S4), encoding (S1) and (S2), respectively. Sequences of (IIb) are given in the specification; they may encode a constitutively active version of a TAO polypeptide.

Preparation: cDNA from rat brain was subjected to two rounds of polymerase chain reaction using degenerate oligonucleotides (sequences given in the specification) derived from the Ste20 sequence. The resulting 420 bp amplicon was labeled and used to screen a cDNA library from adult rat forebrain RNA. Over 100 positive clones were identified and sequence (1) was assembled from two clones. Screening the library for clones at the 5'-end of TAO1 indicated presence of the closely related TAO2 sequence (S2). Sequences (IIb) are human expressed sequence tags, derived from retinal mRNA and represent the human equivalent of TAO1. Once isolated, these sequences (or their fragments) may be expressed in usual vector/host systems, optionally in the form of fusion proteins.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Methods: In methods (k) and (l), MEK3 is preferably activated or phosphorylated. To identify (A), a test compound is incubated with (I) or (Ib) and the effect of the compound on MEK3-phosphorylating activity is determined, e.g. from incorporation of **32P** from labeled adenosine triphosphate. Alternatively, the test is carried out in a cell that expresses a reporter gene, expression of which depends on MEK3 activation. In treatment methods, MAb, or its fragments, or nucleic acid is used to inhibit or increase MEK3 phosphorylation.

Preparation: MAb are produced by usual methods of immunization and cell fusion.

L24 ANSWER 16 OF 22 WPIDS (C) 2003 THOMSON DERWENT

AN 1998-086644 [08] WPIDS

DNN N1998-068832 DNC C1998-029283

TI **Assaying phosphatidyl inositol** 3,4,5-tris phosphate in a sample - by converting it to inositol 1,3,4,5-tetrakis phosphate by alkaline hydrolysis, then measuring the amount of the tetrakis phosphate.

DC B04 K08 S03

IN BATTY, I H; DOWNES, P C; VAN DER KAAY, J

PA (UYDU-N) UNIV DUNDEE

CYC 79

PI WO 9749990 A1 19971231 (199808)* EN 35p

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9731836 A 19980114 (199822)

EP 918990 A1 19990602 (199926) EN
R: CH DE DK FR GB IT LI NL SE
JP 2000513091 W 20001003 (200052) 30p
ADT WO 9749990 A1 WO 1997-GB1673 19970623; AU 9731836 A AU 1997-31836 19970623; EP 918990 A1 EP 1997-927287 19970623, WO 1997-GB1673 19970623; JP 2000513091 W WO 1997-GB1673 19970623, JP 1998-502528 19970623
FDT AU 9731836 A Based on WO 9749990; EP 918990 A1 Based on WO 9749990; JP 2000513091 W Based on WO 9749990
PRAI GB 1996-13107 19960621
AB WO 9749990 A UPAB: 19980223
The following are claimed: (A) **assaying** **phosphatidylinositol** 3, 4, 5-trisphosphate (IP3) in a sample, comprising: (a) converting IP3 present in the sample to inositol 1, 3, 4, 5-tetrakisphosphate (IP4); and (b) measuring the amount of IP4; (B) use of a compound which selectively binds IP4 in an **assay** for IP3; (C) kit of parts for **assaying** IP3, comprising: (a) radiolabelled IP4; (b) a compound which selectively binds IP4; and optionally (c) IP3; (D) kit of parts for **assaying** IP4, comprising: (a) radiolabelled IP4; (b) non-radiolabelled IP4; and (c) a pure protein which selectively binds IP4; and (E) substrate for a **scintillation** proximity **assay**, comprising a **scintillant** and a compound which selectively binds IP4.

USE - IP3 is a second messenger which is the principal product of the receptor-regulated enzyme PI 3-kinase.

ADVANTAGE - The process is straightforward, highly specific and sensitive method which allows the detection of picomolar amounts of (I).

Dwg.0/1

L24 ANSWER 17 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1998-018045 [02] WPIDS
DNC C1998-006639
TI New liposome reagents for detection of analytes - comprise liposome(s) with associated analyte-binding ligand and hapten which can bind to a receptor on a solid phase or in a detection system.
DC B04 D16
IN LARUE, C; MAXFIELD WILSON, N
PA (SNFI) PASTEUR SANOFI DIAGNOSTICS SA; (SNFI) PASTEUR SANOFI DIAGNOSTICS
CYC 77
PI WO 9739736 A1 19971030 (199802)* EN 74p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9728078 A 19971112 (199811)
US 5776487 A 19980707 (199834)
EP 1021166 A1 20000726 (200037) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000509494 W 20000725 (200041) 55p
ADT WO 9739736 A1 WO 1997-US6748 19970418; AU 9728078 A AU 1997-28078 19970418; US 5776487 A US 1996-634969 19960419; EP 1021166 A1 EP 1997-922395 19970418, WO 1997-US6748 19970418; JP 2000509494 W JP 1997-538297 19970418, WO 1997-US6748 19970418
FDT AU 9728078 A Based on WO 9739736; EP 1021166 A1 Based on WO 9739736; JP 2000509494 W Based on WO 9739736
PRAI US 1996-634969 19960419
AB WO 9739736 A UPAB: 19980112
The following are claimed: (A) a liposome reagent for use in an **assay** to detect an analyte in a test sample comprising: (a) a liposome; (b) a ligand chosen to bind specifically to the analyte and

associated with the liposome membrane, and (c) a haptenated component associated with the liposome membrane, where the hapten is chosen to bind specifically to either a receptor on a solid phase or to a component of the signal detection system used in the **assay**; and where the ligand and haptenated component remain associated with a portion of the bilayer to maintain a linkage between the solid phase and ligand; (B) a method for determining the presence or amount of analyte in a test sample comprising: (a) contacting the liposome reagent with test sample and the solid phase having the receptor to the hapten immobilised on it, simultaneously or sequentially for a time for the analyte in the sample to bind to ligand in the liposome reagent and for the liposome reagent to bind to the receptor on the solid phase, and (b) detecting the presence or amount of analyte bound to the solid phase; (C) a kit for use in the **assay** to determine the presence or amount of analyte present in a test sample comprising the liposome reagent and a labelled detector for analyte; (D) a liposomal soluble support matrix for use in an **assay** to detect analyte in a test sample comprising: (a) a first liposome reagent comprising a liposome having a ligand chosen to bind specifically to an analyte in a test sample, where the ligand is associated with the liposome membrane; and a haptenated component associated with the liposome membrane, where the hapten is selected to bind specifically to a receptor; and (b) a second liposome reagent comprising a liposome having the receptor where during the **assay** the haptenated component on the first liposome reagent binds the receptor on the second liposome reagent to form the soluble support matrix; (E) a liposomal soluble support matrix for use in an **assay** to detect analyte in a test sample, comprising a liposome reagent comprising a liposome, a ligand chosen to bind specifically to the analyte and associated with the liposome membrane, a haptenated component associated with the liposome membrane, where the hapten is chosen to bind specifically to a receptor, and where during the **assay** receptor is added to bind the haptenated component and form the solid soluble support matrix, and (F) a kit for use in an **assay** to determine the presence or amount of analyte present in a test sample comprising: (a) ligand-bearing haptenated liposome reagent capable of binding to analyte present in a test sample; (b) a receptor capable of binding to the hapten on the haptenated liposome reagent; (c) a receptor-bearing solid phase, and (d) labelled detector for analyte detection.

The solid phase may be e.g. microtitre plates, polystyrene beads, magnetic particles, nitrocellulose strips, membranes, latex microparticles, and particles prepared from hydrocarbon polymers including polystyrene and polypropylene, glass, metals and gels. The liposome may be formed from e.g. cardiolipin (CL), **phosphatidylinositol**, phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine, shinogomyelin, phosphatidic acid or dipalmitoylphosphatidyl ethanolamine (DPPE). The hapten is preferably **biotin** and the receptor may be neutravidin, streptavidin, **avidin** or antibody capable of specifically binding to **biotin**. The bound analyte may be detected using a reagent conjugated to a **label**, e.g. alkaline **phosphatase** (ALP) or horseradish peroxidase.

USE - The products and methods can be used for the detection of analytes such as antibodies to an autoimmune determinant or antibodies to an allergen.

ADVANTAGE - The use of liposomes provides for the ligand to be intercalated into a fluid gel-type matrix which can allow steric flexibility and increased binding capacity to an analyte, thereby providing high sensitivity.

Dwg.0/0

L24 ANSWER 18 OF 22 WPIDS (C) 2003 THOMSON DERWENT

AN 1997-536008 [49] WPIDS
DNN N1997-446167 DNC C1997-171476
TI Detection reagent for diagnostic determination of anti-phospholipid antibodies - comprising liposome with specific ligand for analyte in its membrane and haptenated component that binds immobilised or labelled receptor.
DC B04 D16 S03
IN LARUE; C; MAXFIELD WILSON; N
PA (SNFI) PASTEUR SANOFI DIAGNOSTICS SA; (BIRA) BIO-RAD PASTEUR; (SNFI) PASTEUR SANOFI DIAGNOSTICS
CYC 77
PI WO 9740387 A1 19971030 (199749)* EN 58p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9727340 A 19971112 (199811)
US 5780319 A 19980714 (199835)
EP 900382 A1 19990310 (199914) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000509492 W 20000725 (200041) 43p
EP 900382 B1 20020807 (200259) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69714584 E 20020912 (200268)
ADT WO 9740387 A1 WO 1997-US6448 19970418; AU 9727340 A AU 1997-27340 19970418; US 5780319 A US 1996-636733 19960419; EP 900382 A1 EP 1997-921243 19970418, WO 1997-US6448 19970418; JP 2000509492 W JP 1997-538188 19970418, WO 1997-US6448 19970418; EP 900382 B1 EP 1997-921243 19970418, WO 1997-US6448 19970418; DE 69714584 E DE 1997-614584 19970418, EP 1997-921243 19970418, WO 1997-US6448 19970418
FDT AU 9727340 A Based on WO 9740387; EP 900382 A1 Based on WO 9740387; JP 2000509492 W Based on WO 9740387; EP 900382 B1 Based on WO 9740387; DE 69714584 E Based on EP 900382, Based on WO 9740387
PRAI US 1996-636733 19960419
AB WO 9740387 A UPAB: 19971211
A reagent (I) for detecting an analyte (A) comprises: (i) liposome; (ii) ligand (L) specific for (A) and associated with the liposome membrane, and (iii) haptenated component (HC), also associated with the membrane, in which the hapten binds specifically to either an immobilised hapten receptor (HR) or to a HR on a label that is one part of a signal detection system. The liposome is constructed so that during **assay** L and HC remain associated with a portion of the membrane, maintaining a link between the solid phase and L. Also claimed are: (1) an **assay** for detection of an analyte in a test sample by using (I), and (2) kits containing (I).

Ab are recognised by using an anionic phospholipid (PL) as L, specifically cardiolipin (CL), **phosphatidylinositol**, phosphatidylserine or phosphatidic acid. HC is a haptenated (particularly **biotinylated**) PL, e.g. as above or phosphatidylethanolamine (PE) or sphingomyelin, best dipalmitoyl-PE (DPPE). Preferred HR is a goat anti-**biotin** antibody bound to a solid phase via donkey anti-goat antibodies. Preferred labels are enzymes, especially horseradish peroxidase or alkaline phosphatase (AP), and the solid phase is a test tube, microtitre plate well, particle (particularly magnetic) or nitrocellulose strip. For determination of Ab, (I) also includes beta -2-glycoprotein I (II), which may enhance bonding of anionic PL to Ab, or (II) is added to the mixture of sample and (I).

USE - (I) is used specifically to detect anti-phospholipid antibodies (Ab) which are present in cases of primary anti-phospholipid syndrome,

systemic lupus erythematosus, human immunodeficiency virus infection and syphilis where they are implicated in recurrent thrombosis, spontaneous abortion and thrombocytopaenia.

ADVANTAGE - The **assays** do not require an encapsulated receptor (so maintenance of liposome integrity is not essential) and compared with enzyme-linked immunosorbent **assay**, the method provides increased binding capacity and steric flexibility, with better retention of the native structure of the ligand. Detergents can be tolerated in the **assay** mixture and binding through the liposome membrane maximises the efficiency of L-A recognition. The **assay** is well suited to automation. When stored at 4 deg. C under nitrogen, (I) remain usable for over 16 months.

Dwg.0/0

L24 ANSWER 19 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1997-526477 [48] WPIDS
DNC C1997-167534
TI Screening **assay** for antifungal agent - based on inhibition of checkpoint protein kinase catalysed phosphorylation.
DC B04 C07 D16
IN FOSTEL, J M; LUCA, F C; STEINER, E M; WINEY, M E
PA (ABBO) ABBOTT LAB; (UYTE-N) UNIV TECHNOLOGY CORP
CYC 20
PI WO 9739143 A2 19971023 (199748)* EN 22p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX
ADT WO 9739143 A2 WO 1997-US6304 19970417
PRAI US 1996-633617 19960417
AB WO 9739143 A UPAB: 19971222
The following are claimed: (1) identifying antifungal agents, comprising combining a checkpoint protein kinase (CpPK) with a test compound, catalysing **phosphorylation** of a **kinase substrate** with the combination and determining the extent of phosphorylation; (2) polypeptide comprising the 764 residue amino acid sequence given in the specification, or an enzymatically active fragment or derivative; (3) DNA plasmid comprising a nucleotide sequence encoding the polypeptide; and (4) treating fungal infections by administering a specific inhibitor of a fungal CpPK.

USE - The polypeptide, which is a unique component of fungal cells, is a CpPK designated Mps1p ''monopole spindle''. Mps1p is a dual specificity protein kinase encoded by the Saccharomyces cerevisiae MPS1 gene, which is essential in 2 aspects of yeast cell growth, namely duplication of the spindle body, and arrest of the cell cycle at a critical checkpoint in the presence of microtubule damage or loss of spindle integrity. Msp1p is therefore useful as an intracellular target for antifungal drug therapy, as well as a target in **assays** for the identification of agents which act specifically on Msp1p.

Dwg.0/2

L24 ANSWER 20 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1994-009540 [02] WPIDS
DNC C1994-003868
TI Prepn. of (gamma-**32P**)-**labelled** nucleoside tri **phosphate** - from di hydroxy-acetone phosphate, **32P** -inorganic phosphate and a nucleoside di phosphate.
DC B02 B03 D16 K08
IN LIN, P
PA (ICNC) ICN BIOMEDICALS INC
CYC 19
PI EP 577266 A2 19940105 (199402)* EN 11p

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CA 2097386 A 19931202 (199408)
JP 06062884 A 19940308 (199414) 8p
EP 577266 A3 19941130 (199536)
ADT EP 577266 A2 EP 1993-304251 19930601; CA 2097386 A CA 1993-2097386 19930531; JP 06062884 A JP 1993-130500 19930601; EP 577266 A3 EP 1993-304251 19930601
PRAI US 1992-891593 19920601
AB EP 577266 A UPAB: 19940223
A method for preparing (-gamma-**32P**)-labelled nucleoside triphosphates (NTPs) by enzymatic reactions is claimed comprising (a) combining dihydroxyacetone phosphate (DHAP), (**32p**)-inorganic phosphate (32Pi) and a nucleoside diphosphate (NDP) in a reaction mixt., (b) adding to the reaction mixt. conversion enzymes triosephosphate isomerase (TPI), glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and 3-**phosphoglycerate kinase** (PGK) to facilitate enzymatic reactions and (c) adding to the reaction mixt. during the enzymatic reactions beta-nicotinamide adenine dinucleotide (beta-NAD+) together with oxaloacetic acid and malate dehydrogenase (MDH) to recycle NAD+ from its reduced form of nicotinamide adenine dinucleotide (NADH). The NDP may be e.g. adenosine 5'-diphosphate (ADP), 2'-deoxyadenosine 5'-diphosphate (dADP), guanosine 5'-diphosphate (ADP), cytidine 5'-diphosphate (CDP) or 2'-deoxythymidine 5'-diphosphate (dTDP). The reaction mixt. pref. contains 200-350 mM Tris-HCl (pHG) and 30-60 mM MgCl2.
USE/ADVANTAGE - The method is used for effectively **labelling** the gamma-**phosphate** gp. of nucleotides. It produces (**32P**)-labelled NTPs with high specific activity in high yields without producing unwanted **32P**-labelled contaminants. The prods. are used for labelling nucleic acids and for studying and **assaying** enzyme reactions.
Dwg.0/1

L24 ANSWER 21 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1991-310056 [42] WPIDS
DNC C1991-134276
TI Diagnosis of HSV infections by NMR - using F-19-labelled tri fluoro-thymidine, which undergoes phosphorylation by HSV-induced thymidine kinase.
DC B03 B04 K08
IN BODOR, N S; BREY, W; RAND, K H
PA (UYFL) UNIV FLORIDA
CYC 1
PI US 5053215 A 19911001 (199142)*
ADT US 5053215 A US 1988-199354 19880526
PRAI US 1988-199354 19880526
AB US 5053215 A UPAB: 19930928
The phosphorylated F-19 trifluorothymidine can be **assayed** by NMR spectroscopy.
USE/ADVANTAGE - The method provides an alternative to brain biopsy, hitherto the only reliable way of diagnosing HSV encephalitis (a life-threatening condition which affects a small number of HSV patients). Similarly, the technique can also be used to diagnose disseminated infection in the newborn. Dose is intravenous, and the drug is administered with e.g., saline, isotonic dextrose, or buffers contg. NaH2PO4 or Na2HPO4 with ethyl alcohol, propylene glycol, benzyl alcohol, etc..
0/4

L24 ANSWER 22 OF 22 WPIDS (C) 2003 THOMSON DERWENT
AN 1990-178355 [23] WPIDS

DNC C1990-077457
TI Highly specific **assay** for protein kinase C - using peptide **substrate** which is **phosphorylated** by protein **kinase** C and radio labelled ATP.
DC B04 D16 J04
IN GALLIS, B M
PA (IMMV) IMMUNEX CORP
CYC 1
PI US 4923802 A 19900508 (199023)*
ADT US 4923802 A US 1985-744498 19850613
PRAI US 1985-744498 19850613
AB US 4923802 A UPAB: 19930928

Assaying for the presence of protein kinase C (pkC) comprises (a) reacting activated pkC in the presence of ATP with a peptide substrate of formula (I)-(IV) H2N-(A)n-X-(A)n-COOH (I), H2N-(B)n-X2-(A)n-X1-(A)n-COOH (II), H2N-(A)n-X1-(A)n-X3-(C)n-COOH (III), and H2N-(B)n-(A)n-X1-(A)n-X3-(C)n-COOH (IV). In the formulae each A, B, C independently = a basic amino acid residue; n = 1-5; X1 = Ser or Thr. X2, X3 = 1-4 amino residues of any compsn. except X1. Also claimed in a packaged kit for **assaying** pkC comprising (i) labelled ATP in a first container; (ii) agents for activating pkC in a second container; and (iii) a peptide of formula (I)-(IV) in a third container.

USE - pkC phosphorylates basic and other types of proteins causing a functional change of the protein, typically a decrease or increase in enzymatic activity and possibly plays a role in the activities of tumour promoters such as phorbol diesters. The **assay** provides a method of detecting, characterisation and purificn. of pkC.

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